A JOHNS HOPKINS PRESS HEALTH BOOK

Caring for Children Who Have

SEVERE NEUROLOGICAL IMPAIRMENT

A Life with Grace

JULIE M. HAUER, M.D.

VISIT…

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Note to the Reader: This book was not written about *your child* and is not meant to substitute for medical care of your child. Treatment plans for individual children who have severe neurological impairment must be based on a dialogue between the physician and the patient and his or her family. Our book is intended to help with that dialogue.

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Foreword

Dear Parents and Family Members, Clinicians and Friends,

I imagine that you opened this book because a child you love or care for—or both, as is most often the case—is living with severe neurological impairment, and you are looking for knowledge, help, guidance. Take heart: while no single source can provide all the information you might want, in the pages that follow you are going to find much that will be valuable in your efforts to provide the best care possible for this child.

The realities of children living with severe neurological impairment are twofold: a side of difficulties and dark moments, and a side of joy and light. Dr. Julie Hauer attends to both sides in this book, as she has done for every patient and family she has encountered over the years of her career as an esteemed and beloved physician devoted to the care of children with major medical problems. A self-proclaimed introvert from Minnesota, Julie is soft-spoken but vibrant when discussing the care of patients, and she combines the intellect of an expert with the warm-hearted empathy of an extrovert. Over the years, as I have come to know her as a trusted colleague, collaborating on several projects, I have learned much from her ideas about how to take better care of these children who have so many medical problems, and I have been captivated by her idealism of what good care can achieve.

Let me here acknowledge a wish that we all most likely share—that this child did not have this condition or these problems, or that this condition could be cured, completely and forever. I feel this wish well up within me every time I take care of a child who has suffered a severe brain injury, or experiences intractable seizures, or is diagnosed with a tumor or a brain malformation, or has a progressive neurological disease. A large part of my career has been focused on trying to prevent these conditions and cure children who have these conditions. Yet, given the state of our medical knowledge and technology, including a vast array of medications and

surgical procedures, many of these conditions cannot currently be cured, and while I fervently hope for the day when more cures become possible, in the meantime, children with these conditions need to be cared for, in a way respecting the reality of their situation and the great value of their lives. And in this undertaking of caring even when cure is not possible, I have found great hopes—for a better quality of life, for improved function, for less discomfort, for more time with family at home—and across this vast range of hopes that patients and their families value, I have witnessed the remarkable accomplishments that are possible, especially when we work together with a common sense of purpose and vision.

On the difficult side of living with severe neurologic impairment, this book is the best encyclopedia available regarding the problems these children encounter, and the best guide on how to think about, evaluate, and deal with these problems.

Some of the information needed to understand what is going on in the brain or in the rest of the body is, unavoidably, quite detailed and specific and laced with some medical terms. So, too, for descriptions of medications or surgical interventions or tests. For readers who are not familiar with the concepts or terms that Dr. Hauer uses, this book can be a primer on medical language and ideas that will enable parents and family members to talk with medical personnel and advocate for their child.

Guiding the reader through this information, Dr. Hauer is always very clearly organized, promoting, by example, an organized approach to addressing any medical problem that arises in the child's life. Additionally, her advice is always both grounded in the best available scientific or medical evidence (which is often, sadly, quite limited) and extremely pragmatic. No aspect of care is unimportant, no detail too small. If you are struggling with a tough decision, there is probably useful advice in the pages that follow. If your child has a jejunostomy feeding tube that is acting up, you'll find three different methods to try—and three to avoid. If your child appears to be in pain and the source and thus the solution are unclear, an orderly, stepwise process of evaluation and potentially empirical trials of therapy is laid out.

Case vignettes and studies, which appear throughout the book, bring many of the common problems and dilemmas to life. From difficult seizure management or discomfort with feeding to deciding whether to have a tracheostomy tube inserted—all of these challenges and more are illustrated, both in terms of the dilemmas and in terms of potential solutions. In tandem with these vignettes are a host of "key points" and tables to make finding or retrieving information efficient.

On the other side of these children's lives are love and laughter. Dr. Hauer quotes a parent who says that "you don't need to prepare for joy"—and joy there is, not all of the time, for sure, but often. Parents have told me how small, lovely things catch them off guard and take their breath away. The journey these parents take with their children has many unexpected turns but also surprising twists, some deep downs but also graceful ups. One goal of better medical care is to tip the balance more in favor of these high points, by improving the health status of the child and by empowering parents and clinicians to feel more capable of meeting the challenges that the children confront.

There is one last thing we should discuss: most children with severe neurological impairment have shortened lives. This aspect of their reality is so hard to think about. Parents have shared with me their sometimes overwhelming feelings of fear, dread, and sadness when thinking about the future. And as this entire book makes plain, there is much that can be done to help these children, whatever their life span will be, to have the best life possible. If medication can really help them, give it; if surgery can really help them, do it. Still, there may come a time when more medicine will actually help less or even potentially hurt, when surgery may be likely to do more harm than good. This is a time, not to give up, but to fight on for important goals, focusing on the child's comfort and quality of life. The final chapter is dedicated to this part of the mission of providing outstanding, loving care to these children. To do this requires more courage than most parents know they had. The point I would want to bring out, as gently as I can, is that confronting the sadness may prevent some badness that can ensue from medical care that does not keep the whole patient in view, that starts simply to do things to the child, but no longer for the child.

So, I hope this book helps you on your quest to provide the best care possible for the child you love and care for. I hope that it spurs the work that we—parents as well as physicians and researchers—need to do, so that in a few years, Dr. Hauer can revise this book and rightly label it "new and improved." And I hope that it provides you with companionship, a sense of connection to others who share a commitment to children, with their impairments and their perfections.

Chris Feudtner, MD, PhD, MPH
Pediatric Advanced Care Team
The Children's Hospital of Philadelphia

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Preface

It is only with the heart that one can see clearly;
what is essential is invisible to the eye.
—Antoine de Saint-Exupéry

I started my journey in the medical care of children who have severe neurological impairment (SNI) in 1995. The most remarkable individuals I have met on this journey are the parents. They have been my best teachers, through their thoughtful questions and their loving decisions made on behalf of their children. Parents help us understand the value and meaning of their child's life and how they feel that they are better for the experiences brought to them by their child.

I wrote this book with several goals in mind. One goal is to provide a comprehensive summary of what we know about the medical care needs of such children. It is important to have this information brought together so as to increase awareness of how one problem may impact another and may involve various specialty areas. Are the problems with tube feedings a problem with motility, with visceral pain, or with the autonomic function or vomiting center of the brain? Are the episodes of arching and arm straightening a spasticity problem or a pain problem?

Another goal is to integrate the benefits of palliative care more seamlessly into the care of these children. This can help improve a child's comfort throughout life and eliminate a common view of "treating" versus "keeping comfortable." My goal is to integrate this by providing guidelines for medical care and for symptom treatment and a framework for decision making. This reflects my years of providing medical care for children who have SNI, my work in palliative care, and my focus on the aspects of pain and symptom treatment that are unique to children who have SNI. Essentially, how can we utilize the "best" that the worlds of medicine and palliative care have to offer?

In writing this book, I do not presume to be the voice of parents. I have tried to represent parents through the many case examples. I have also

tried to cover questions asked of parents and worries that are sometimes not asked about.

The term *SNI* is used throughout the book to indicate a group of children. What is not indicated by this term is what each child *can* do, as it implies only what the child *can't* do. Each child will have his or her own personality, likes, dislikes, and meaningful connections to others. In medicine, we at times miss opportunities to celebrate and find meaning with families as we focus our efforts on not missing a medical problem that we can potentially improve.

I outline here some of the themes that are important to this book.

THE "VOICE" OF THIS BOOK

The book provides information with a more clinical "voice." The hope is that this information will help guide parents and guardians in finding their individual voice. Parents can use the information to help identify questions to ask the healthcare team and to help frame the options presented. This stronger clinical focus can give the impression that decision making is a logical process. Yet, the emotional part of decision making—that is, how the heart and the head influence each other—is as important as the factual information discussed in this book.

The book is also written to be useful for healthcare providers involved in the care of children who have SNI. The medical literature is referenced so that physicians and nurse practitioners will know the sources of information I have used. Other providers, including nurses, social workers, and case managers, may find the book helpful as they provide care for children and support for families.

INFORMATION THAT CAN EMPOWER PARENTS DOES NOT REPLACE THE ROLE OF A CHILD'S PHYSICIAN

The best information available cannot replace the care provided by a trusted physician. A relationship between a parent and a trusted physician often includes openness to information that may not be part of routine care, such as details about identifying pain and treating distressing symptoms. The information in this book is intended for many children, yet does not determine when specific information is relevant for an individual child.

EMPOWERING PARENTAL EXPERTISE

This book is based on the premise that families are in the best position to determine how their child is or is not benefiting from what can be done medically. Parents are in the best position to determine the "quality" of their child's life and therefore how the child may potentially benefit from medical interventions. This can be challenging when physicians are seeing a child at a time of illness and not seeing the child in his or her typical environment. Fortunately, more medical training programs are now including home visits, to increase understanding and awareness of what we do not see when a child is in an unnatural environment. Parents are also in the best position to determine when medical options may be less likely to help or more likely to be burdensome. This can also be challenging for parents, given the subjective and emotional nature of "harm," "burden," and "suffering."

DUALITY

Parents encounter many dual themes. Parents celebrate the meaningfulness of their child's life along with managing the "chronic sorrow" about what their child cannot do. Parents often balance hope while also preparing for what may happen. There is also the duality of the potential benefit of medical interventions as well as the potential for harm and prolonged suffering. In addition, there is the common use by healthcare providers of *doing well* that requires the context of what *well* means. Attending to the dual nature of these and other themes is beneficial, yet takes more intellectual and emotional effort.

SUPPORTING A RANGE OF DECISIONS

Parents should feel supported in all decisions. A supportive environment will ensure support of the "best" decision, as there is often no "right" decision. This book intends to contribute to this goal of a supportive environment by providing a summary of information along with approaches to framing this information.

USE OF EVIDENCE

Evidence that is specific to children who have SNI is used as much as possible, and evidence related to adults with similar problems is used

when necessary. Literature is referenced to ensure a transparent process of informing. Suggestions are provided for framing information when the evidence does not indicate certain benefit, with consideration given to potential harm.

CASE EXAMPLES

Many of the specific examples in this book represent decisions not to use a medical intervention that could be used. These case examples are not included because they represent the "right" decision; rather, they are selected to highlight why parents make such decisions. This is based on the observation that parents often find it emotionally harder and more difficult to find words when considering to not use or to discontinue an intervention. It is naturally easier to celebrate success from an intervention. A decision to protect a child from an intervention that might result in harm or suffering is not routinely considered a decision to "celebrate," yet the reason for the decision is the same—love for one's child.

ETHICAL DECISION MAKING

Ethical decision making represents principles for all children. Information is framed in this book using the ethical principles that help guide what decisions can be made. Parents are in the best position to make decisions that are ethically allowed, with rare exceptions. This reflects the reality that a child (or an adult dependent on others for care and decision making) does not exist in isolation but is part of a family and community. Decision making exists within these ethical principles and is guided by the values of the family and community. Ethical principles in North America include the following points (Canadian Paediatric Society, Bioethics Committee, 2004, www.cps.ca/en/documents/position/treatment-decisions).

Determining the best interests for the child or adolescent must include "careful consideration given to:

- Chances of survival;
- The harms and the benefits of treatment;
- Evidence regarding long- and short-term medical outcomes of the treatment; and
- Long-term implications for the child or adolescent's suffering and quality of life."

Decisions not to use life-sustaining medical treatment can occur when there is a "high degree of probability that:

- There is irreversible progression to imminent death;
- Treatment is clearly ineffective or harmful;
- Life will be severely shortened regardless of treatment, and the limitation or withdrawal of interventions will allow greater palliative and comfort care;
- Lives will be filled with intolerable distress and suffering that cannot be prevented or alleviated."

DISABILITY AND CHRONIC COMPLEX CARE

Children who have SNI straddle two worlds: the world of disability and the world of chronic complex care. One is the world of functional limitation; the other is the world of medical complexity. This group of children is part of both worlds. They often interface with the medical world, not because they are disabled, but because of the associated medical problems. Many of the medical problems reviewed in this book are a result of the impaired central nervous system (CNS). When medical decisions are encountered and reviewed by medical teams, some physicians may focus excessively on the disability, or it may *feel* as if the decision is being considered because of the disability, rather than how the problem affects the child's health and comfort.

Too commonly, these two worlds get mixed up and misunderstood. To avoid confusion, which can lead to misunderstanding, it is helpful to recognize different groups with overlapping challenges and needs. Considering such groups serves to illustrate differences, yet it is critical to consider an individual beyond the points illustrated by each group. An individual is always so much more than what any label can convey.

Children who have SNI have severe physical and intellectual impairment. They have severe limitations in communication, though most communicate in a manner that can be understood by those close to the child, such as showing a consistent response that indicates enjoyment from specific activities. These children remain dependent on others for all care needs and decision making throughout life. The term *severe neurological impairment* is often used for these children to reflect the global aspect of this impairment. Many of the associated medical problems occur as a result of the CNS impairment. These problems cannot be "fixed," yet interventions

can modify their long-term effects. Such problems commonly result in a shortened life span.

In contrast to this group of children are people who have physical disability and normal intellectual ability that allows the capacity for decision making. Another group consists of people with intellectual disability and no significant physical impairment, with some acquiring the ability to participate in decision making through assent. In both groups, medical problems are typically less frequent during childhood than in children who have SNI, unless associated with a specific diagnosis, and the life span is often similar or closer to that of "normally developing" adults.

The distinction between disability and medical complexity is highlighted now so as to minimize the fear of a discrimination against disability that will affect medical decision making. This fear can result in the unintended harm of physical suffering, when "everything" is done out of fear of discrimination. Just as everyone has a right to equal access to all healthcare options and to choose interventions that others have a right to, everyone also has a right to limit medical interventions that can become too burdensome. The goal is to ensure equal access for all to all intervention options. Equal access to care does not determine when such care should be used.

VULNERABILITY

Children who have SNI remain vulnerable to experiencing distressing symptoms that remain unrecognized and untreated. Information about symptom assessment and treatment for children with SNI has been available only in the past decade. We also become susceptible to viewing symptoms in these children as "this is what she is like."

Parents of such children are vulnerable to being misunderstood. As an example, a mother was considered neglectful when she did not visit her daughter every day in the hospital, and she was subsequently reported to child protective services. One of the child's home care nurses later explained, "She felt so helpless seeing her daughter cry every day, something that had been increasing for months prior to this hospitalization. Not until the symptom expert got involved and her daughter's comfort finally improved after almost four weeks in the hospital did she realize what a bad mom she felt like for not being able to tolerate her daughter's crying. Improving the comfort of this girl has completely changed this family, allowing others to see what a good mom she is and decreasing the distress of her brother."

Children who have SNI are also vulnerable to "overtreatment" as a result of good intent. It is challenging to distinguish between when something can be improved and when it is an irreversible problem. Information is provided in this book as a guide to such considerations, both medical features of the child and approaches to framing decisions about care.

"PRUNING" BACK MEDICAL TREATMENT THAT IS BURDENSOME

Medical care has enhanced the lives of countless children who have SNI. Medical treatment options can also be a burden in many circumstances. For anyone with a chronic condition, medicine can become an overgrown plant that can take over the garden, if not scrutinized and pruned back when needed. Decision making is the process that helps determine what to prune and what to keep.

MEDICATIONS

Medications are indicated by their generic name, with the trade name in parentheses. The trade names are included so as to help parents recognize medication names. This does not reflect a recommendation of a trade-named over a generic medicine when a generic formulation is available. Many of the medications mentioned in the book involve off-label use, as they have not been studied in children who have SNI. Multiple sources were used for information about medications.

EACH CHILD IS AT A DIFFERENT STAGE

The information in this book covers all stages of life of a child who has SNI. It includes "routine" care interventions that can be beneficial for many years, new problems that respond readily to interventions, declining benefit from chronic and acute treatment interventions, and end-of-life care. Reading information before it is relevant to your child may elicit strong emotions and worries. Put the book aside as needed, or ask a trusted family member or friend to read for information that may be helpful. When your child is doing well, celebrate! Know there is information here when needed.

Comments about coping are best represented by this parent, writing on the topic "Coping with Neurological Impairment."

"First, I let myself be sad sometimes. Second, I take breaks. Third, I have a good support system. In the end, it's about figuring out what works for you. There's not a 'For Dummies' book available when you have a child with a neurological impairment. Parenting will not be like you expected it to be or like what you've experienced with your other children.

There will be times when simply making it through the day is the best you can do. There will be days when you think that if you hear another person tell you what a 'strong person' you are, you'll snap.

My life is a work in progress. I get through it one day at a time, or sometimes, one minute at a time. I rejoice in the positives and I mourn when I need to. At the end of the day I try to remember this quote by Maya Angelou: 'You did what you knew how to do, and when you knew better, you did better'" (L. Kelly, *Complex Child E-Magazine*, 2008, http://articles.complexchild.com/dec2008/00094.html).

I WISH FOR YOU AND YOUR CHILD what we typically want for ourselves: life enhanced to its best potential, treated with dignity, and honored throughout.

Acknowledgments

I am indebted to many people for the lessons learned and the support provided. They made this book possible. First and foremost are the parents, guardians, caregivers, and children who inspired me to write the book. It is one thing to write about the care needs and decisions encountered. It is another thing to live them. The level of expertise, love, and compassion of the families is both humbling and inspiring.

I am grateful for my years as a medical educator, including my time with pediatric residents, as well as with the parents who challenge our thoughts on behalf of their children. The care provided to children who have complex chronic conditions is only as good as the ability to describe this care to others and the ability to be receptive to other approaches. I am grateful to those involved in my own education during my pediatric residency, including my continuity clinic preceptors Mark Butterbrodt, MD, and Chuck Oberg, MD, as well as Michael Shannon, MD, the residency program director during my residency training. I also had the good fortune to work with remarkable educators during my time as residency program director, including Margie Hogan, MD, and Joseph Sockalosky, MD, along with the many chief residents who enhanced the training experience of many in the program.

I have worked with many exceptional individuals since my residency. Pam Heggie, MD, provided knowledge that was instrumental early on in my care of children who have severe neurological impairment; she is an exceptional role model in how to provide care and advocate for the children and families. Henry Staub, MD, exemplified everything that is right about pediatrics; I am blessed to have worked with him in my early years in pediatrics.

There are many key individuals in the years I worked at Gillette Children's Specialty Healthcare. I am indebted to Reverend Helen O'Brien. She touches families in remarkable ways and brings outstanding experience from the bedside that enhances her expertise in the areas of pediatric

palliative care and ethics. I have learned much from her and have benefited from her graceful and supportive presence. I wish to also acknowledge Jean Stansbury, RN, MS, CPNP; Melanie Rouse, LICSW; Kara Pittman, LICSW; Melissa Connolly, LICSW; Elayne Sommers, CCLS; and Don Postema, MTS, MPhil, PhD.

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Caring for Children Who Have
SEVERE NEUROLOGICAL IMPAIRMENT

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CHAPTER 1

Caring for a Child Who Has Severe Neurological Impairment

An Overview

I do not at all understand the mystery of grace—only that it meets us where we are but does not leave us where it found us.

—Anne Lamott

Here are three different "definitions" of *grace*:

1. A disposition to act with love, kindness, and compassion
2. Unmerited divine assistance given to humans for their regeneration or sacred purpose
3. A girl with severe neurological impairment with no known cause who, despite the limitations caused by her disease, had an amazing life made possible by her parents, sister, caregivers, and healthcare team, until her death at age 5½ years

Families of children who have severe neurological impairment (SNI) are the heart and soul of their child's care. They navigate a world of emotion and uncertainty and are asked to enter the medical world of logic and reason. The two worlds can, at times, seem at odds, and yet both worlds want what is best for the child.

"I wouldn't choose this, but I wouldn't have it any other way" is a sentiment many families express. Caring for children and adults with SNI exposes both families and healthcare providers to the power and beauty of humanity. The healthcare provider may bear witness to "ordinary" families doing extraordinary things. Such families may view what they do as "you do what you have to; others would do the same." Others can only wonder at "what it takes" to provide such herculean efforts of care, to ensure such a well-lived life for one's child, and at the loving yet difficult decisions

made. Families may be humbled by the kindness and commitment of others yet frustrated at how some people "don't get it."

WHY THIS BOOK? MEETING THE NEEDS OF CHILDREN AND YOUNG ADULTS WHO HAVE SNI

This book provides detailed and practical evidence-based guidelines for the complex medical care needs of children and adults who have SNI. It is written to be helpful for families and healthcare providers involved in caring for such individuals. The intent is to empower parents with information so they have a full understanding of the options and approaches for each problem their child may encounter. This understanding can help parents identify questions and gather information to share with their child's healthcare providers.

The theme that runs through this book is the importance of integrating accurate knowledge with the goals and values of the family as a guide to care plans. Care plans can be designed with the following aims:

- Maintain the best health and function of the child
- Minimize any decline in health
- Maximize recovery from acute illness
- Minimize unintended problems
- Protect against interventions that can prolong suffering
- Maintain comfort throughout

With an understanding of the importance of comfort, this book integrates state-of-the-art symptom management into the medical care of many problems.

The healthcare options reviewed in this book are balanced with a sensitive acknowledgment of limits in the intended benefit of interventions. I include strategies for decision making when the benefit of an intervention is uncertain. This emphasis on integration of medical care and symptom management plans, along with frameworks for decision making, is in keeping with the needs of families—by maximizing their understanding of options and supporting their decisions with compassionate and effective care. Detailed guidelines are provided that allow the individualization of care plans to the specific needs of each person.

Before considering the care needs, it is helpful to understand how children and adults who have SNI are vulnerable to many challenges, and this understanding is expressed best by parents.

They ask us what we want to do, but when we give them our answer, it is clear it is not the decision they wanted. They ask as if we get to make the choice, but they act differently. You can see it in their face, body language, and how they keep asking us the same question, as if we might change our mind.

In the hospital, it is amazing how many little things they change in my child's care. Like my child's tube feedings. They act like there is a specific way that feedings have to be given. Do they feed their children (without feeding tubes) like that at home? Of course not; you learn to observe your child's patterns and cues. And of course a child misses a meal every now and then. Why is this treated so differently in my son, just because he has a feeding tube? They need to recognize you can't control everything, just like I've come to accept that at home. Where's the common sense?

My son's medical team is wonderful. They clearly care and always listen to my concerns. What is hard is how often I hear "I don't know" or "we'll figure it out when it happens." I know they will be there for me, but I never feel settled. I'm not looking for someone to fix my son, and I know that no one can tell me exactly what will happen, but how will I know when enough is enough? I guess I would just like the possible scenarios spelled out, because I do better when I know what to expect.

When my daughter has a serious respiratory illness, I am always asked, "Do you want us to intubate your daughter if she can't breathe on her own?" I say yes, because I don't want her to suffer, but I'm not sure if it is the best decision. They say, "We will keep her comfortable if you don't want us to intubate her," like I have to sign her up for a death sentence. Basically, I'm confused and scared.

I am afraid to talk to the medical team about what I don't want done to my son. I worry that they will stop trying as hard to provide him with good care. He is still benefiting from the treatment plans we have in place. I'm not ready to give up on him yet.

As medicine's understanding of the components of good care and our systems of care continue to improve, not every child or family encounters such challenges. But many families do remain vulnerable to these challenges. As highlighted by these and other parent comments, as well as comments in the literature that focuses on children who have SNI, parents may experience many of the following:

- Uncertainty
- "Navigating uncharted territory"
- Becoming experts out of need
- Parental expertise being minimized or disregarded
- Lack of clarity about who has decision-making power
- Lost control
- Navigating through the care of many specialists
- Limited information about many neurological diseases
- Guilt about the cause of the disease
- Guilt about decisions (Steele 2002, 2005)

As parents become familiar with their child's needs, including how these needs can change with time, they often learn to navigate hope, meaning, loss, and uncertainty. At such times, parents can be observed as simultaneously hoping for what is possible, wishing for what is not likely, and preparing for unwanted changes.

Other challenges include lack of evidence for medical decision making and problems with managing symptoms. These challenges are further compounded by personal and regional bias about care decisions. As two physicians recently wrote, "Providers may consciously or unconsciously impart their own views through their framing of facts, potential outcomes, options, and recommendations to obtain decisions aligned with their own beliefs and values. Many ICUs, hospitals, and geographic regions have their own treatment 'signatures,' reflecting historical norms and entrenched practice patterns" (Holloway and Quill 2010). And though pain and other symptoms occur frequently, many healthcare providers find it challenging to identify, let alone treat, discomfort and distress in nonverbal children and adults who have SNI. Even experts in pediatric symptom management indicate that the greatest anxiety they encounter includes how to care for the nonverbal child in distress, not being able to identify the cause of pain and vomiting, and managing muscle spasms and abnormal movements (McCluggage 2006).

In the context of these challenges, it is easy to forget that families often find meaning, hope, and joy in the experience of providing care. Successes may be "measured" differently in different families, but they do exist for many families. In addition, families may speak of the lessons learned through their child and the important role of this child in their family. Healthcare providers should never miss opportunities to celebrate each success, as families navigate their child's needs.

Healthcare mandates for chronic conditions

When my son is sick with a respiratory illness, they treat it like a new problem and insist that he needs to be seen in the clinic or in the ER. He is always treated with an antibiotic, usually right away, otherwise, later, when he doesn't get better. We know why he becomes sick each time, so why does he need to be seen to start treatment? I get it that you can't routinely start on antibiotic without determining if it is needed. That would make sense for my healthy son, as he has no risk to being sick. But we know that aspiration is the source of the problem in my other son and that the treatment for this is an antibiotic.

Parents have greater access to information about healthcare options for their child than ever before. Excellent professional Internet sites offer medical definitions and advice, and parent support groups share information about all kinds of topics, including clinical trials that may benefit a child who has a specific disease. This increased access is taking place at the same time as a growing mandate to examine the quality of healthcare and the systems that deliver this care. To address the healthcare needs of all, and especially those who have the most complex chronic conditions, elements of care continue to evolve and be defined. Examples include the fundamental need for care that is family centered and care delivery based on the principles of the medical home model. These examples define the need for care that is coordinated, continuous, comprehensive, and accessible, with families empowered to be the center of all decisions about care.

Such changes can create either tension or partnerships, as families and healthcare providers navigate shifting medical models. Tension can occur if families do not feel listened to as they share insights into their child; physicians may feel their role is not respected if their recommendations seem to be disregarded. It's noteworthy that both parties are experiencing the same challenge: how to have their expertise respected and utilized. Ideally, a partnership of trust and mutual respect develops between parents and healthcare providers, with each understanding what the other brings to the table. At its best, a partnership will include physicians trusting the "eyes" of parents as the experts in their child's needs, and parents benefiting from the knowledge and experience of a physician who cares for many children with similar problems. A mutual understanding of the information relevant to a child's care needs can enhance the success of such partnerships.

With this information in mind, we can see that children who have SNI are ideally cared for by a team that has expertise in anticipating and managing the problems and the care needs of these children and their families. This team includes a physician with knowledge in the management of all the healthcare needs of an individual who has SNI. Experts in providing for the supportive needs of families also must be available, either as members of the child's healthcare team or through the community.

Goals of this book

This book reviews the complex problems of children who have SNI. For parents, it provides access to comprehensive, evidence-based information about their child's current and potential healthcare needs—along with an understanding that parents must balance their need for information with their need to be a parent. As parents have greater access to information, they risk becoming hypervigilant and feeling responsible for all medical details. Parents are reminded, at different points in the book, how to think broadly about a problem; I then provide details for parents to review with their child's healthcare providers. One of the goals of this book is to provide parents with comprehensive access to information when they need it, to help enhance their roles as parents.

Another goal is to assist the primary care physicians, complex care specialists, and subspecialists involved in the care of children who have SNI. There is a growing need for chronic care specialists with expertise in all of the management practices reviewed in this book, rather than providers who coordinate care across multiple specialists. Specialists provide important expertise for specific problems, but they often lack a broader context of the many interrelated problems that cross specialties.

This book supports the various care needs, challenges, and healthcare mandates in a variety of ways. It intends to accomplish the following:

- Provide an evidence-based review for each care need, including approaches to chronic and acute management
- Empower parents of children and adults who have SNI to become experts in the complex chronic care needs of their child
- Provide practical care plans that can be readily applied to daily patient care needs, including in the child's home or community setting of care
- Increase recognition and knowledge of all care plan options, including home-based plans

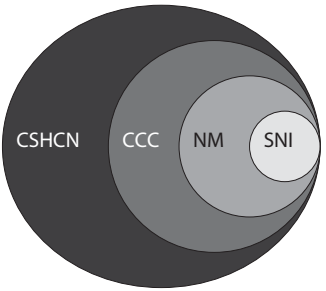
- Utilize this information to minimize bias in how options are considered and presented
- Provide guidelines for assessing pain and other symptoms, along with state-of-the-art treatment plans for each symptom
- Enhance a partnership of shared knowledge between families and physicians
- Empower families with information and in identifying strengths
- Facilitate decision making, including the use of tools for framing decisions
- Minimize problems that can occur out of good intent, such as the risk of drug reactions as more medications are used (polypharmacy) and the risk of harm from an intervention used out of a need to "do something"
- Summarize information in each chapter, including "Take-home points"

WHO IS THIS BOOK ABOUT?

This book addresses the care needs of children who have severe impairment of the brain, referred to as severe impairment of the central nervous system (CNS). Children with such impairment are at risk for the problems reviewed throughout this book. To indicate this group, these individuals are referred to as *children who have SNI.* However, the information is also relevant to adults who have SNI acquired in childhood.

A child may have impairment of the CNS for many reasons, as covered in detail in chapter 2. In general, the impairment may be a result of damage to the brain (due to lack of oxygen, traumatic brain injury, or infection) or may be associated with a specific medical diagnosis (such as a genetic disorder, metabolic disease, or structural abnormality of the brain).

This group of children is sometimes described by other terms, including terms used in epidemiologic studies and in debating and setting healthcare policy. These terms include *children who have special healthcare needs* (CSHCN) and *children who have complex chronic conditions* (CCC). Other terms include *medically complex children* or *medically fragile children.* Medically complex children have been described as children seen by multiple specialists, children who often are dependent on technology for basic needs such as feeding and whose optimal care involves coordination across inpatient and outpatient settings (Simon et al. 2010). Figure 1.1 summarizes some of the terms used and shows where categories overlap.



Category	Definitions and comments
CSHCN Children with special health care needs	Children "who have or are at increased risk for a chronic physical, developmental, behavioral, or emotional condition and who also require health and related services of a type or amount beyond that required by children generally." (McPherson et al. 1998)
CCC Complex chronic conditions	"Any medical condition that can be reasonably expected to last at least 12 months (unless death intervenes) and to involve either several different organ systems or 1 system severely enough to require specialty pediatric care and probably some period of hospitalization in a tertiary care center." (Feudtner, Christakis, and Connell 2000)
NM Neuromuscular disorders	Brain and spinal cord malformations, mental retardation, central nervous system degeneration and disease, infantile cerebral palsy, epilepsy, muscular dystrophies and myopathies, i.e., diseases of the CNS, lower motor neuron, and muscles. (Feudtner, Christakis, and Connell 2000)
SNI Severe neurological impairment	Impairment of the central nervous system (CNS) from any cause: structural abnormality of the CNS, lack of oxygen to the CNS, infection, genetic disorder with associated impairment, metabolic disease.

Figure 1.1. Categories used to describe children who have complex chronic conditions.

Children in the CCC category can be further subdivided by the primary condition: neuromuscular (NM), metabolic, congenital or genetic, respiratory, cardiac, renal, gastrointestinal, hematologic, or immunologic conditions, and malignancy (Feudtner, Christakis, and Connell 2000). A child with SNI may have several problems, such as a primary genetic disorder with associated neuromuscular (brain malformation), cardiac (heart malformation), and respiratory (chronic respiratory disease) problems. This information is summarized in recognition of how children are defined for eligibility in state programs and for the purposes of research.

For this book, I selected the designation *SNI* in recognition of the problems that may be encountered by a child who has any condition that involves impairment of the CNS. Though there are some similar care needs and challenges with lower motor neuron diseases such as spinal muscular atrophy (SMA) and muscle diseases such as Duchenne muscular dystrophy (DMD) and congenital myopathies, there are also some important differences:

- Similarities include some of the information given in chapters 6 and 9.
- There may be differences in the benefit and risk of certain interventions, such as Nissen fundoplication as an intervention for gastroesophageal reflux disease (GERD). As an example, the risk of retching and pain following fundoplication may be much greater in children with impairment of the CNS than in children without such impairment. In addition, it is not clear whether fundoplication benefits one of these groups of children more than the other.
- There are many problems associated with impairment of the CNS that would not be encountered in the lower motor neuron and muscle diseases. These include the increased risk of seizures, spasticity, muscle spasms, autonomic dysfunction, central neuropathic pain, alterations in homeostasis, and precocious puberty.
- Given both the differences between these groups and the rarity of many of the conditions, there may be benefit in research that looks, collectively, at diseases of the CNS rather than at neuromuscular diseases that include both central and peripheral diseases of the nervous system.

CARE DELIVERY: PROVIDERS, LOCATIONS, AND MODELS OF CARE

The complexity of care needs for children who have SNI often means that multiple healthcare providers are called on for help with the individual problems encountered. There is growing recognition that such complex care is improved when it is centralized, coordinated, and family centered. To meet these recognized needs for improved care, the concept of a *medical home* was identified as a model of care for children who have chronic healthcare needs.

I find it hard to know who to call when I have a concern. Everyone is so nice, but often I'm told, "So and so will need to address that question," yet that person

isn't available or doesn't have the answer. We have good access to care, and great specialists, but I sometimes worry about who has the big picture in mind. Everyone seems to have a good grasp of their piece of the picture, without understanding how different recommendations have a domino effect on other problems. I guess that's why I need to be my son's expert.

Medical home

The American Academy of Pediatrics (AAP) has defined the medical home as a model of care delivery that is accessible, continuous, comprehensive, family centered, coordinated, compassionate, and culturally effective (AAP 2004). It is not a specific location of care but rather an approach to providing comprehensive care. The care that is provided should be "delivered or directed by well-trained physicians who provide primary care and help to manage and facilitate essentially all aspects of pediatric care." This model refers to how care should be delivered to all children, not just children with special healthcare needs; however, children who have complex healthcare needs are less likely to receive care in this manner (Strickland et al. 2011; Wood et al. 2009).

Providing this level of coordinated care requires a broad base of knowledge of both the medical care and the resources to assist with care needs. This includes the ability to anticipate and identify medical problems, the management of each problem, the availability of medical specialists with sufficient expertise to provide input as needed, and community resources that meet the nonmedical needs of the child and family.

Creating a team of experts

In the medical home model, the goal is for one physician, such as the child's primary care pediatrician, to directly manage and facilitate all aspects of the child's care. This approach often means that other individuals, such as a case manager, are employed to assist with identifying other needs for the child and family, supplying information about community resources to meet these needs, and coordinating and communicating the child's care plan. For some children, the arrangement may include medical experts in complex chronic care.

Chapters 3 through 8 review problems for which children who have SNI are at risk, along with the management of those problems, based on available evidence. For children who have SNI, the need for expert input

in managing some of these problems means that a large number of specialists are often involved in the child's care.

In this book, the term *physician* is most commonly used. A care team may also include other medical providers, such as nurse practitioners. The term *healthcare provider* refers to all disciplines, including nurses, social workers, physicians, and therapists. Tables 1.1 and 1.2 summarize the experts who might be part of the child's medical care team.

Coordination of care for complex chronic conditions

In the clinic, it feels like most problems are addressed by a referral to a specialist or as "let's wait and see." In the hospital it becomes an urgent decision for problems that my son has been dealing with chronically. And I wish they could see how well he does at home. It seems they base their decisions only on their small window into my son's life. And yet I get no better guidance outside of the hospital.

The more complex the child's care needs, the more challenging it is to ensure a medical home with seamless care across multiple care providers and various sites (Strickland et al. 2011; Wood et al. 2009). Other challenges include acute assessment made in the emergency department and hospitalizations occurring when physicians do not know the family or are not familiar with care options in the community. The care "in the moment" and for the specific problem may be exceptional, but it may not take into account the chronic care of the child and family.

With such a rich array of experts, families are at risk for fragmented care when a clear line of communication has not been established and the role of each player is not defined. Too often, there is no one physician with the expertise to consider and prioritize each individual medical problem and the recommendations from each specialist. In addition, there is a risk that the medical needs will remain the focus, with the psychosocial and spiritual needs of the family going unrecognized and the community resources available to meet such needs not being utilized (Wood et al. 2009). Too often, families then face diminished physical, emotional, and spiritual energy to provide care, process information, and prioritize goals for their child.

In addition to primary and specialty medical care, children who have SNI and their families may receive supportive services that are tied to a variety of systems or funding agencies. Provision of services and funding can further fragment care when case managers from different systems

TABLE 1.1 Medical providers

Expert	Problems commonly assessed and managed
Neurologist	• Initial diagnosis; seizures and other problems (e.g., spasticity, autonomic dysfunction, dystonia)
Gastroenterologist	• Gastroesophageal reflux disease (GERD), motility disorders, constipation • Placement of percutaneous endoscopic gastrostomy (PEG) tube
Pulmonologist	• Chronic respiratory disease as a result of pulmonary aspiration and other contributing problems
Sleep medicine specialist	• Obstructive and central sleep apnea
Otolaryngologist	• Tracheostomy placement • Salivary duct ligation and gland excision
General surgeon	• Gastrostomy feeding tube (G tube) placement • Nissen fundoplication
Physical medicine and rehabilitation specialist	• Spasticity management, including botulinum toxin (Botox) injection • Salivary gland Botox injection • Assessment of hip subluxation • Assistance with durable medical equipment
Orthopedic specialist	• Hip subluxation, neuromuscular scoliosis
Neurosurgeon	• Ventriculoperitoneal (VP) shunts, intrathecal baclofen (ITB) pumps, vagus nerve stimulator (VNS)
Endocrinologist	• Precocious (early) puberty
Geneticist	• Initial diagnostic evaluation and identification of associated abnormalities • Genetic counseling for parents and other family members
Metabolic specialist	• Initial diagnostic evaluation • Management of metabolic disease, including acute metabolic crisis
Palliative medicine specialist	• Assessment and management of pain and other symptoms (vomiting, retching, feeding intolerance, dyspnea) • Assistance with decision making through interdisciplinary support

TABLE 1.2 Other healthcare providers

Dietitian	• Assesses nutritional requirements: calories, protein, vitamins, minerals • Assists with specialized diets: ketogenic diet for epilepsy, diets for specific metabolic disorders
Pharmacist	• Assesses for medications with duplicate or competing receptor properties, alterations in drug metabolism, and other drug-drug interactions when a new medication is prescribed
Therapists: physical, occupational, speech	• Identify options for durable medical equipment (DME): wheelchairs, seating, orthotics, standers, and transfer, positioning, and bathing equipment • Assess feeding and swallowing
Nurses: inpatient and home-based	• Assist with bedside assessment of pain and other distressing symptoms • Listen in "real time" during times of emotional and spiritual distress • Facilitate communication between families and physicians
Social workers	• Provide emotional support, psychosocial assessment, and supportive counseling in collaboration with other providers • Link families to mental health resources in the local community • Anticipate legal and financial needs (guardianship, government programs that cover some medical expenses, special needs trust) • Access providers for these and other needs, such as DME
Child life specialists	• Assist siblings with fears about having a sister or brother who has complex healthcare needs • Assist families with memory making and the legacy of a child • Provide education around appropriate grief responses of children
Chaplains	• Support faith traditions and spiritual values that promote healing and hope

(continued)

TABLE 1.2 *(continued)*

• Support families as they face loss or grief • Identify religious and cultural factors that can shape how a family faces illness, suffering, and decision making • Provide a supportive presence

become involved, such as with a medical home, hospital, agency, or health plan payer. Partnerships have been developed to create complementary rather than duplicative or competing efforts. As an example of a collaborative model, developed through the Seattle Pediatric Palliative Care Project, co-case managers were identified by the health plan (health plan case manager) and by the project team selected from a home health agency in the patient's community (nurse case manager) (Hays et al. 2006). To meet many of these challenges and the healthcare delivery mandates, there is a need for experts in the care needs of children and adults who have SNI. In terms of medical needs, the physician providing continuity of care should have expert knowledge in the common, chronic and acute problems encountered. In other words, the medical home model is more than coordination of care; it reflects expertise of care. Such expertise includes an understanding of all the problems that must be anticipated and the various management options to consider.

Ideally, a complex chronic care expert can manage such problems as respiratory, gastrointestinal, growth and nutrition, and endocrine conditions, as well as alterations in homeostasis. Other problems clearly require a higher level of training to manage over the long term, including management of seizures by neurologists and of metabolic diseases by metabolic specialists. Other problems require assessment and management as identified along the way. The necessary specialties may include sleep medicine for evaluation of a possible sleep disorder; otolaryngology when considering a tracheotomy or salivary duct procedure; general surgery for Nissen fundoplication; physical medicine and rehabilitation (PM&R) for spasticity management with botulinum toxin type A (Botox) injections; and PM&R and neurosurgery for consideration of an intrathecal baclofen pump. In later chapters I discuss how an expert in complex chronic care can provide broad knowledge of management options for each problem, a longitudinal perspective of the child's health trajectory, and an ongoing relationship with the family that recognizes their goals and values that will factor into decision making.

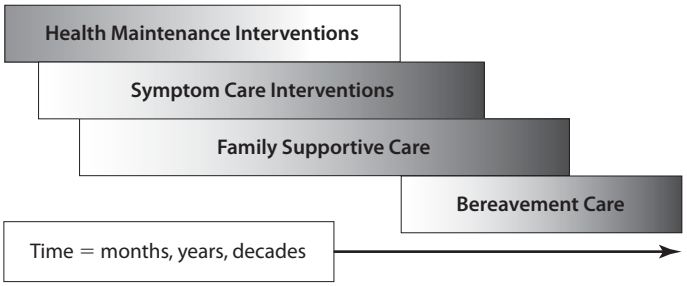


Figure 1.2. Changing needs of the child and family.

Finally, it is essential to recognize how the needs of the child and family can shift over time, as summarized in figure 1.2. This figure points to the importance of "nonmedical" healthcare providers in the ongoing care needs of the child and family.

Constructs of care

In addition to the medical home model, other care constructs have been defined that are essential to the needs of children who have SNI and their families. These include family-centered care, multidisciplinary and interdisciplinary care, and palliative care.

Every time my daughter is in the hospital, some of the nurses freak out when she has a seizure and the neurology team wants to change her seizure medications. I know they want to help, but I know from experience that another medication combo will not make it better and might make it worse, especially with the side effects. If I can manage this as a parent at home, why can't they handle the fact that it won't get better, it's just a seizure, she is doing OK and we are happy with her care? Why don't they listen to me?

Family-centered care

Family-centered care is grounded in "collaboration among patients, families, physicians, nurses, and other professionals for the planning, delivery, and evaluation of health care" (AAP 2003). This partnership can be considered a foundation of care. Here are some of the guiding principles of family-centered care:

- Understanding that the family is the child's primary source of strength and support
- Respecting each child and his or her family
- Honoring racial, ethnic, cultural, and socioeconomic diversity and its effect on the family's experience and perception of care
- Recognizing and building on the strengths of each child and family, even in difficult and challenging situations
- Supporting and facilitating choice for the child and family about approaches to care and support
- Sharing honest and unbiased information with families on an ongoing basis and in ways they find useful and affirming
- Providing and/or ensuring formal and informal support (e.g., family-to-family support) for the child and his or her parent(s) and/or guardian(s)
- Collaborating with families at all levels of healthcare
- Empowering each child and family to discover their own strengths, build confidence, and make choices and decisions about their health

Multidisciplinary and interdisciplinary care

Commonly, children who have SNI receive multidisciplinary care, with individual practitioners reporting on what each is doing while working side-by-side but not necessarily together. It is clearly more challenging for children and families to receive interdisciplinary care, in which different professionals work collaboratively to arrive at treatment decisions after an interactive process that considers input from all members.

When challenging treatment plans or decisions are encountered, an ad hoc interdisciplinary team meeting can be arranged, replicating what an interdisciplinary care team provides on a routine basis. Such team meetings benefit from careful planning. This is covered in more detail in chapter 9.

Palliative care

Palliative care is an approach to care that seeks to improve the quality of life of patients who have life-threatening conditions and their families (World Health Organization 2012). It strives to prevent and relieve suffering by identifying and treating pain and other sources of physical distress early, as well as identifying and providing for the psychosocial and spiri-

tual needs of the family. Such a model of care can be of tremendous benefit to children who have SNI and their families. Though not all children and families have access to palliative care, there are a growing number of such programs. When a palliative care team exists in the child's area of care, the greatest barrier to access is the misinformed belief that palliative care is equivalent to end-of-life care. These are the purposes of palliative care:

- Consider the patient and the family as the center of the unit of care
- Provide relief from pain and other distressing symptoms
- Affirm life and regard dying as a normal process
- Intend neither to hasten nor to postpone death
- Integrate the psychological and spiritual aspects of patient care
- Offer a support system to help patients live as actively as possible until death
- Offer a support system to help the family cope during the patient's illness and in their bereavement
- Use a team approach to address the needs of patients and their families, including bereavement counseling, if indicated
- Enhance quality of life, and perhaps also positively influence the course of illness
- Apply care early in the course of illness, in conjunction with other therapies that are intended to prolong life, and include investigations needed to better understand and manage distressing clinical complications

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It seems like everyone wants to see my son as sicker than I think he is. They often ask, "What do you want us to do?" when he is sick. I know they want me to be prepared, but do they think he is so sick that he could die at any time? He is now 5, doing great, has had no serious problems. I start to doubt myself. Am I in denial? If he is that sick, what do I need to know? It seems they are focusing on the decision, yet it seems so abstract. What are the specific things I need to know for now and in the future?

One way to better understand palliative care is to recognize that it supports all treatment options, whether curative, disease modifying, or focused on comfort. When families encounter difficult decisions about intervention options, palliative care is best viewed as focusing on the details and process of decision making, not on promoting a specific decision. The goal is for families to have enough knowledge and support about options to help them in making their decision.

Pediatric palliative care teams are interdisciplinary and include such individuals as a pediatric palliative medicine specialist, a social worker, and a chaplain, along with other experts in the care needs of patients and families. Most pediatric palliative care teams see a large number of children who have SNI. In two different pediatric palliative care programs, as many as 47% to 59% of the patients were likely to have impairment of the CNS, as indicated by such categories as "progressive neurological," "CNS damage," "congenital anomalies," and "genetic or metabolic" (Duncan, Spengler, and Wolfe 2007; Hays et al. 2006).

Palliative care teams often assist with communication, address gaps in coordination, provide access, and empower the family voice in decision making. They also provide benefit by addressing gaps in care delivery. This is possible because such teams are interdisciplinary, are often flexible, such as assisting with care needs in the community and the hospital, and often assist with transitions from one location of care to another.

GOALS AND PHILOSOPHY OF CARE

My daughter is sick and in the hospital every month, and every time we are asked, "What do you want us to do if she stops breathing?" I know what I want and I know what I don't want, I just don't know what happens in between. I want her to be held and loved, involved in family activity, to join us for walks in the park, being with us at the dinner table, part of the family. I don't want her hooked up to machines, alive, but not with us.

Goals of care encompass all the views, beliefs, and values that influence all the decisions we make and all the plans of care we follow. The most common examples of goals are the goal of maximizing comfort and the goal of minimizing decline in health with disease-modifying therapy (Tamburro et al. 2011). Goals of care often change, or evolve, over the course of a complex chronic condition. As less benefit is experienced from disease-modifying treatment, the primary goal may shift to improving comfort and not prolonging suffering. Goals may also focus on the location of care; for example, sometimes the child experiences less benefit and greater distress from repeated hospitalizations but continues to benefit from medical care plans carried out in the home.

Clearly, taking the time to identify what is important can provide invaluable guidance in establishing priorities and making decisions. Having a good understanding of the goals of care lessens worry about "giving up," decreases the sense of needing to "do something" (see below), and

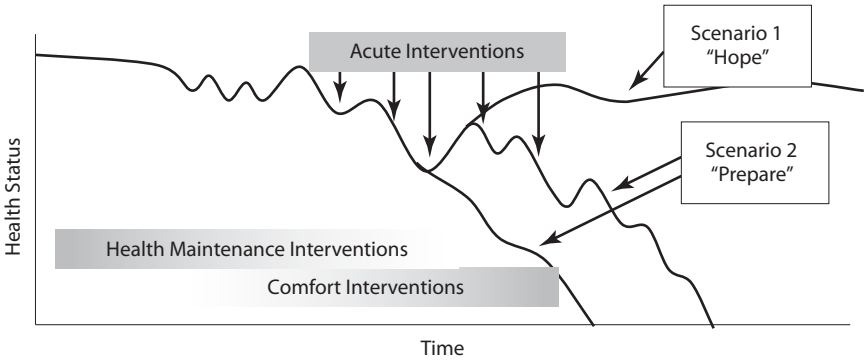


Figure 1.3. Hypothetical trajectories for children who have SNI. *Used with permission of Oxford University Press; adapted from figure 26.2 in J. M. Hauer and K. W. Faulkner, "Neurological and Neuromuscular Conditions and Symptoms," in A. Goldman, R. Hain, and S. Liben (eds.),* Oxford Textbook of Palliative Care for Children, *2nd ed. (Oxford: Oxford University Press, 2012), p. 306.*

enhances choosing how to live. As many parents express it, having this guide helps them know "when I am doing *for* versus doing *to* my child."

Open lines of communication are essential if the goals are to be understood by everyone involved in the patient's care. Many children who have SNI live for years and decades with the goal being to maintain comfort, health, and function and to minimize decline. As time goes on, treatment decisions may focus completely on providing comfort for the child. How goals are prioritized can shift as the ability to meet each goal shifts, as illustrated in figure 1.3.

Many families find it beneficial to discuss and establish an overriding philosophy of care. There is a spectrum of approaches to the care of children who have SNI, from the wish to use invasive interventions in the hospital that may extend life to a focus on care that can occur in the home. Both approaches are equally valid.

A philosophy of care along with goals of care are grounding principles, used to guide decisions early on and as they arise. Just as with goals of care, the philosophy of care can change for a family as their child's condition changes and as their experience and knowledge evolves.

THE BIAS OF LANGUAGE AND THE DESIRE TO "DO SOMETHING"

In this book, I review many interventions that can be considered but are not required. Bias comes into play when such interventions are

presented as being necessary. "Not doing" can be perceived as giving up or not trying hard enough. This is probably the hardest bias to contemplate, because "doing something" is the focus of medicine (what can we do?) as well as of advocacy groups (making sure no child is treated differently from any other).

There is no intention in this book to indicate that one approach is better than another; rather, my intention is to give all options equal weight. It is important to recognize the risk of bias, such as physicians and parents being more likely to view doing "something" as better than doing "nothing." There is no equally weighted voice that "advocates" for the loving decisions made by parents to focus on good care that minimizes the use of invasive interventions. This leaves all parents vulnerable to feeling like "bad parents" when they consider not pursuing a certain surgery or treatment. Ideally, decisions are approached in a fair and balanced—in an unbiased—manner.

This approach should not be seen as conflicting with advocacy for equal access irrespective of the disability, as this advocacy has benefited many children. Instead, it is intended to ensure that good care for all should not restrict what that care looks like for any one individual. Unintended harm of physical suffering can occur when "everything" is done out of fear of discrimination. Equal access to all healthcare options includes the right to limit medical interventions that can become too burdensome. One family viewed this as the difference in choosing something from the regular menu versus the special of the day: "No choice is better, just different."

Many physicians find it easier to focus on specific interventions rather than on presenting the full range of choices that can be made lovingly by families. Reviewing a range of options increases the chance that a family will misunderstand a physician as recommending the option of "giving up." There is no "perfect" way to approach how information is provided or how decisions are considered. As with any professional or personal relationship, when parents trust the person helping them make decisions, misunderstandings can be minimized.

This book begins by discussing the medical problems that occur in children who have SNI, including treatment options based on available evidence. Following these medically oriented chapters, chapter 9 focuses on the process of decision making when considering surgical and invasive interventions. The chapter is intended to explain what can be done and, further, to help parents consider what makes best sense.

I use case examples to illustrate the information in this book. These include examples of medical care plans and the kinds of decisions made by

parents. Many case examples highlight decisions not to utilize a particular intervention that lacks evidence and may not meet the goals of care identified for a child. Such examples do not represent a view of one decision being a "better" decision. Instead, they recognize that parents are more likely to hear other parents share stories about interventions that have been used; they may feel alone and hesitant to share when considering not to use an intervention, out of fear of judgment. When an intervention with uncertain benefit is used and has the hoped-for outcome, it is something to celebrate. In contrast, a decision to protect a child from an intervention with uncertain benefit and potential for harm may not feel like something to "celebrate," yet the reason for the decision is the same—love for one's child.

THE ROLE OF HOPE

Hope is some extraordinary spiritual grace that God gives us to control our fears, not to oust them.
—Vincent McNabb

Hope can serve as an adaptive response to a stressful circumstance, allowing a person to cope. As an example, a parent may hope for a miracle or cure, while making decisions based on the observation that current treatment is prolonging suffering. The concept of giving parents permission to maintain hope while considering "what if" is illustrated in figure 1.3.

A parent's hope can be misunderstood as "being in denial" and "not getting it," if the meaning behind such thoughts is not explored in a nonjudgmental manner. In addition, many parents believe that it is their responsibility, as a "good parent," to demonstrate that they will not "give up" on their child.

Healthcare providers can minimize creating a divide by recognizing the meaning and benefit of hope and by supporting an environment that understands the benefit of hope. Social workers and chaplains can help everyone grasp the deeper meaning behind the words of parents and make sure the healthcare team supports parents' hope.

TYING IT ALL TOGETHER: IT TAKES A VILLAGE

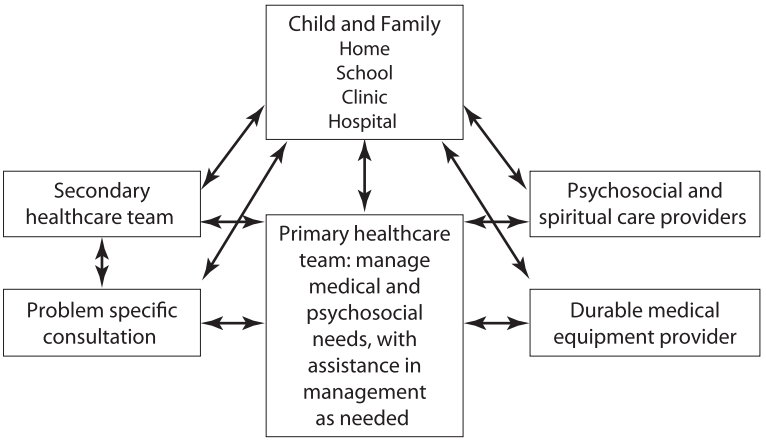
Principles of care for children who have SNI and their families ideally utilize the models of family-centered care, medical home, and palliative care:

- The patient and the family are the center of the unit of care.
- The family is recognized as the constant in the child's life.
- Care is accessible, continuous, comprehensive, coordinated, and compassionate.
- Families are empowered to discover their own strengths, build confidence, and make choices and decisions about their child's health.
- Families and professionals work together in the best interest of the child and the family.
- Communication and information sharing are open and objective.
- The strengths and expertise of all are respected.
- Decision making is shared.
- Pain and other distressing symptoms are identified and treated.
- Psychosocial needs are identified and managed with the use of community resources.
- Cultural diversity and family traditions are honored.
- Family-to-family support is encouraged.
- Successes are celebrated.

Children who have SNI often have a large "village" of healthcare providers. All too often, families struggle with identifying a "point person" for contact. It can be unclear at times which physician or team to call on with a question, and parents who contact one team may be directed to contact someone else to address the concern raised. This approach increases the need to use the hospital for complex care management. It can be detrimental to the child if someone does not have broad expertise in the multitude of medical problems encountered in children with SNI and has no knowledge of the child's health trajectory and the family's goals for their child.

Ideally, the following information is identified, coordinated, and communicated by the primary healthcare team, after clarification of plans with the involved specialists, and is updated as needed:

- Clearly delineate the structure of the care team.
- Anticipate acute problems for families.
- Identify management plans for acute problems expected to recur (e.g., seizure, respiratory illness, autonomic storm, feeding intolerance, and discomfort).
- Clarify the goals of care that guide the development of these care plans.



Primary healthcare team: point of contact unless indicated for specific care needs

- Physicians and nurse practitioners: complex care experts with knowledge of problems to anticipate and management options for those identified, knowledge of a family's goals of care, and knowledge of a child's health trajectory, with use of all information to assist with decision making
    - — Primary person may change as the goals of care change
    - — May involve co-management, especially through transitions
    - — Individuals include primary care pediatricians, complex chronic care experts, and palliative and hospice medicine specialists
- Nurses: clinic and home care
- Social workers: outpatient- or inpatient-based
- Other: may include such individuals as a case manager or interdisciplinary members of a palliative care team

Secondary healthcare team: chronic problems requiring ongoing specialty expertise

- Seizures: neurologist
- Metabolic disease management: metabolic specialist

Problem-specific consultation (examples):

- Evaluation for obstructive or central apnea: sleep medicine specialist or pulmonologist
- Tracheotomy for airway obstruction: otolaryngologist
- Nissen fundoplication: general surgeon
- Spasticity: physical medicine and rehabilitation specialist for botulinum toxin injection and assessment for intrathecal baclofen
- Hip subluxation and neuromuscular scoliosis: orthopedic surgeons

Psychosocial and spiritual needs: social worker, chaplain, child-life specialists

- Such services may be more readily available during hospitalizations; it is important to have a process of communication back to the community-based healthcare team

Figure 1.4. Roles and connections among different team members.

TABLE 1.3 Suggested guidelines for parents

Choosing a doctor

- Seek providers with whom you are comfortable.
- Factors to consider include experience and approachability. Some doctors have experience in caring for children with chronic medical conditions; these doctors are sometimes referred to as "complex care" experts.
- Ask whether the clinic supports a "medical home" model of care.
- Consider how the physician approaches decision making. Ask how the physician feels about parents taking a shared role in decision making.
- If needed, seek out another doctor that better fits your needs. As in all relationships, not all styles (doctor and patient) are right for each other.

Preparing for a clinic appointment

- Trust your experience and knowledge of your child: you may not realize how valuable this is to your child's medical care. It is critically important that you share with healthcare providers what you know and observe about your child. Rely on your sense of when to seek more information. Never be reluctant to ask how your child is doing, how a medicine is working, or what to expect from a treatment.
- If you know you will need extra time for your visit, tell the clinic about this need when you call.
- Make a list of your questions and concerns. Decide which are most important to you.

Getting the most out of the clinic visit

- Bring a list of your top questions or concerns to discuss at every visit.
- Take notes, using the same notebook to write down your questions and the answers at each appointment.
- Bring someone along who can help listen, take notes, and provide support if needed.
- Don't be intimidated. It's okay to ask for something to be explained. It's also okay to respectfully disagree.
- Ask for a written care plan.
- Ask about how to get care after hours (evening and weekends) if needed.

Organizing information

- Make a notebook or folder that holds your child's health information. Include the names of doctors, other caregivers, medicines, etc.
- Keep records of all phone calls, doctor's visits, insurance bills, notices, and forms related to your child. Always take notes, including the date of calls and the person you spoke with. If you're not a good note taker, bring a friend to appointments or use a tape-recorder. Request copies of clinic notes and hospital discharge summaries. Put this paperwork in one place.

TABLE 1.3 *(continued)*

Advocating and caring for your child

- Parents know the needs of their child best, as they are with that child daily. Know that *you* are your child's best advocate. You will have the best sense of what will and won't be helpful for your child.
- Develop strong partnerships with the physicians and other healthcare providers in your child's life. Sharing your expertise about your child will help them provide the best care.
- Connect with another family that has a child with similar needs.
- Caring for your child also means taking care of *you*. Seek out support and ask for help when needed. Support can include care coordinators and in-home nursing. For some families, support comes from using respite care.

Become an expert, yet always remain a parent, first and foremost

- Learn everything you can about your child's diagnosis or condition. Seek experts to assist with this process. Inquire about financial eligibility, free services, and where to get the best care.
- No one can care alone for a child who has SNI. It may seem that no one can provide the same level of care that you can provide for your child. Sometimes it means letting go enough to make sure you can take care of yourself, so you can balance providing care with being a parent.

Note: The following resources were used and are available on the web: "You Are an Advocate for Your Child with Special Health Care Needs!" www.familytiesnv.org/Files/Lcenter/1_YouAreAnAdvocate.pdf; "Families Partnering with Providers," https://org2.democracyinaction.org/o/6739/images/PartneringWithProviders.pdf; "Building Early Intervention Partnerships with Your Child's Doctor: Tips from and for Parents," http://del.wa.gov/publications/esit/docs/ParentTips_English.pdf.

- Communicate care plans to relevant care providers, best achieved with access through electronic medical records.
- Identify the team to call (primary vs. specialty) when questions arise about acute care plans and other complex needs.

Figure 1.4 provides a summary for healthcare teams of how care can be coordinated, with the role of different providers defined. Table 1.3 summarizes information for families as they interface with the child's medical team.

For children who have SNI and associated complex medical problems, a broad-based medical perspective must be available to the family that is in keeping with the family's hopes, goals, and values. The interrelatedness of medical problems and psychosocial needs makes this broad perspective critically important. Decisions must be made in a shared manner, with the

family at the center of decision making guided by the principles of care summarized above, and with expert medical knowledge and tools for framing—as reviewed throughout this book.

OTHER RESOURCES FOR PARENTS

Medical Home Portal, Department of Pediatrics, University of Utah, www.medicalhomeportal.org/living-with-child

Familyvoices.org

Washington State Medical Home, www.medicalhome.org/families

RESOURCES FOR PHYSICIANS

American Academy of Pediatrics National Center for Medical Home Implementation, www.medicalhomeinfo.org

Medical Home Portal, Department of Pediatrics, University of Utah, www.medicalhomeportal.org/clinical-practice

Washington State Medical Home, "Brochure for Doctors and Other Primary Care Providers: What Is a Pediatric Medical Home?" www.medicalhome.org/leadership/documents/PCPbrochurev8.12.2008.pdf

References

AAP (American Academy of Pediatrics) Committee on Hospital Care. 2003. Family-centered care and the pediatrician's role. *Pediatrics* 112(3 Pt 1):691–97.

AAP Medical Home Initiatives for Children with Special Needs Project Advisory Committee. 2004. Policy statement: organizational principles to guide and define the child health care system and/or improve the health of all children. *Pediatrics* 113(5 Suppl): 1545–47.

Duncan J, Spengler E, Wolfe J. 2007. Providing pediatric palliative care: PACT in action. *MCN Am J Matern Child Nurs* 32(5):279–87.

Feudtner C, Christakis DA, Connell FA. 2000. Pediatric deaths attributable to complex chronic conditions: a population-based study of Washington State, 1980–1997. *Pediatrics* 106(1 Pt 2):205–9.

Hays RM, Valentine J, Haynes G, et al. 2006. The Seattle Pediatric Palliative Care Project: effects on family satisfaction and health-related quality of life. *J Palliat Med* 9(3):716–28.

Holloway RG, Quill TE. 2010. Treatment decisions after brain injury—tensions among quality, preference, and cost. *N Engl J Med* 362(19):1757–59.

McCluggage HL. 2006. Symptoms suffered by life-limited children that cause anxiety to UK children's hospice staff. *Int J Palliat Nurs* 12(6):254–58.

McPherson M, Arango P, Fox H, et al. 1998. A new definition of children with special health care needs. *Pediatrics* 102(1 Pt 1):137–40.

Simon TD, Berry J, Feudtner C, et al. 2010. Children with complex chronic conditions in inpatient hospital settings in the United States. *Pediatrics* 126(4):647–55.

Steele R. 2005. Navigating uncharted territory: experiences of families when a child is dying. *J Palliat Care* 21(1):35–43.

Steele RG. 2002. Experiences of families in which a child has a prolonged terminal illness: modifying factors. *Int J Palliat Nurs* 8(9):418–34.

Strickland B, Jones JR, Ghandour RM, et al. 2011. The medical home: health care access and impact for children and youth in the United States. *Pediatrics* 127(4):604–11.

Tamburro RF, Shaffer ML, Hahnlen NC, et al. 2011. Care goals and decisions for children referred to a pediatric palliative care program. *J Palliat Med* 14(5):607–13.

Wood DL, McCaskill QE, Winterbauer N, et al. 2009. A multi-method assessment of satisfaction with services in the medical home by parents of children and youth with special health care needs (CYSHCN). *Matern Child Health J* 13(1):5–17.

World Health Organization. 2012. WHO definition of palliative care. www.who.int/cancer/palliative/definition/en.

CHAPTER 2

Impairment of the Central Nervous System
Specific Conditions

There are things known and there are things unknown,
and in between are the doors of perception.
—Aldous Huxley

A child is so much more than the condition with which he or she is labeled. Even so, having a label, or diagnosis, can be helpful in understanding the present and planning for the future. Recognizing the different types of conditions—the diagnoses, or so-called labels—that affect children by impairing the central nervous system makes it easier to understand the child's medical problems and what symptoms we might see or might anticipate seeing in this child. This chapter reviews information about some specific conditions, as well as conditions collectively, because there is very little information about some diseases and because some children don't have a specific diagnosis.

The conditions that involve impairment of the CNS can be divided into disorders that are "static" and disorders that are "progressive." The term *static* indicates that the CNS impairment is the result of an event or a condition that does not directly cause further damage to the CNS. In contrast, a *progressive* condition refers to ongoing injury to the CNS as a result of the underlying disease.

Static impairment of the CNS can be a developmental disorder, such as cerebral palsy (CP), or can be the result of a specific disease or injury to the CNS. *Cerebral palsy* refers to nonprogressive impairment of the CNS that affects muscle tone and control of movement. CP is not a diagnosis but a developmental label indicating this impairment. Another term occasionally used is *static encephalopathy*, again referring to permanent impairment

of the CNS. The diseases that can result in static impairment of the CNS and are therefore also causes of CP are covered in detail in the first section of this chapter.

The various conditions that result in progressive decline of the CNS are often categorized as either inborn errors of metabolism or metabolic diseases. The resulting neurodegenerative process can involve primarily the gray matter of the brain cortex or the white matter of myelination. The potential problems associated with these conditions are reviewed in the section "Inborn errors of metabolism."

This chapter is not intended to be an exhaustive review of specific conditions, nor does it cover the identification and diagnosis of specific conditions. Such information is well covered elsewhere, including at websites dedicated to specific diseases. Here, I review the types of problems that children who have SNI may encounter; other chapters provide more detail about these problems. Included in this chapter is a summary of the functions of different areas of the brain. This general overview helps us grasp the types of problems that children with impairment of the CNS may have, by describing the complexity of functions controlled and processed by the brain.

The chapter ends with some general comments about prognosis and life expectancy. The important point in this final section is that prognosis is a framework; it is not a prediction for a specific child. While information in this book can increase awareness of what we might anticipate, each child's story will be the best guide to the future.

STATIC IMPAIRMENT OF THE CENTRAL NERVOUS SYSTEM

Problems that can result in static impairment of the CNS include the following (note that these problems are also identified as causes of cerebral palsy):

- Lack of oxygen to the brain, such as from hypoxic ischemic encephalopathy (HIE) in the perinatal period, a near-drowning event, or a cardiac arrest
- Traumatic brain injury (TBI)
- Structural malformations of the brain, such as hydranencephaly or lissencephaly
- Infections of the fetus during pregnancy, such as cytomegalovirus (CMV), or during infancy, such as meningitis or encephalitis
- Genetic conditions with associated CNS impairment

TABLE 2.1 Problems associated with impairment of the CNS

All conditions (static and progressive)
Nutrition: Inadequate oral intake, excessive weight gain and overfeeding with tube feedings
Respiratory: Impaired secretion mobilization, aspiration, decline of pulmonary function
Gastrointestinal (GI): Constipation, gastroesophageal reflux, impaired intestinal motility
Neurological: Spasticity, dystonia, chorea, myoclonus, seizures, autonomic dysfunction, central apnea
Sleep: Obstructive sleep apnea, impaired sleep, altered arousal
Endocrine: Delayed or precocious puberty, hypothyroidism, abnormal sodium regulation
Orthopedic: Hip subluxation, neuromuscular scoliosis (curvature of the spine)
Pain: Nociceptive (tissue injury and inflammation) and neuropathic (central pain, visceral hyperalgesia)
Metabolic and mitochondrial disorders
Vision and hearing: Progressive impairment
Neurological: Motor and cognitive regression, seizures, myoclonus, spasticity, dystonia, chorea, neuropathy, myopathy with muscle weakness and cramps, fatigue, autonomic dysfunction, stroke-like episodes
Respiratory: Aspiration, apnea (obstructive and central)
Cardiac: Cardiomyopathy and cardiac conduction defects
Behavioral: Dementia, agitation, self-injurious behavior, anxiety

The problems that can result from severe impairment of the CNS include abnormal tone and movement, seizures, swallowing difficulties, impaired vision and hearing, and intellectual disability. These and other problems associated with severe static impairment of the CNS are outlined in table 2.1.

Although we are discussing static impairment, we know that some of these children will develop progressive changes in the CNS, referred to as neurodegeneration. Progressive decline may result from cell death of the neurons (nerve cells), known as neuronal apoptosis (Hotchkiss et al. 2009). Several features can suggest a decline in the function of the CNS:

- Changes in a child's level of alertness
- Increased sleeping
- Lower heart rate and temperature
- Changes in the pattern of breathing, including intermittent pauses in breathing
- Changes in intestinal motility
- Increased severity of stiffening, arching, and posturing

Such changes can be transient—they may come and go—or may stabilize at a new baseline, or may be slowly progressive. When considering such changes it is helpful to assess for reversible causes such as medication toxicity, while also considering the potential for progressive irreversible changes in the brain.

Though these progressive changes are not well described in the medical literature, parents have described such features in their children—for example, on a support group web page for parents of children who have hydranencephaly, a condition in which the cerebral hemispheres are absent. Descriptions provided include "most children just keep developing more difficulties and gradually recover less quickly or completely from an illness" and "some just have their whole systems slow down and die" (International Hydranencephaly Support Group, no date). Features described by families include increased frequency of seizures; sleeping more; slowing of heart rate, respirations, and intestinal motility; and lowering of body temperature (Rays of Sunshine, no date). Some children are also described as becoming unresponsive for hours or a few days, though the unresponsiveness was transient in some children.

GENETIC CONDITIONS AND CONGENITAL SYNDROMES

Although it is not possible to provide detailed descriptions of all the genetic conditions with associated SNI that have been identified and defined, a review of two of the more common conditions can highlight some points that are relevant to other genetic conditions. This section includes information about associated problems, such as developmental delay, central apnea, and decision making about surgery for congenital heart defects.

Rett syndrome

Rett syndrome is a neurodevelopmental disorder of young girls, characterized by cognitive impairment, communication dysfunction, stereotypic

movements, and growth failure. The associated disability can range from mild to severe. The diagnostic criteria have been revised and are available at the International Rett Syndrome Foundation (IRSF 2011; Neul et al. 2010). Rett syndrome is caused by a sporadic mutation in the MECP2 gene (methyl-CpG-binding protein 2) on the X chromosome. More than two hundred different mutations have been found on the MECP2 gene, with eight common mutations accounting for the majority of children who have Rett syndrome.

Table 2.2 summarizes the problems associated with Rett syndrome, which may also involve any of the potential problems associated with impairment of the CNS listed in table 2.1. When considering pain as a potential problem in a child who has Rett syndrome, for example, keep in mind that many of these children have a diminished response to pain, but some have an increased sensitivity to "internal" pain, such as abdominal pain (Downs et al. 2010). Also described are screaming spells and inappropriate laughing; gallbladder disease (Percy and Lane 2005); and autonomic dysfunction (Rohdin et al. 2007; Weese-Mayer et al. 2008).

In a child with Rett syndrome who behaves in ways that suggest pain, the physician needs to consider gallstones. Given the other sources of pain behaviors in children with SNI, as reviewed in chapter 4, visceral hyperalgesia and central neuropathic pain, for example, must also be considered. Reasons to consider these pain sources in a child who has Rett syndrome include (1) the description of increased "internal" pain in some children; (2) the identification of thalamic changes, noted as a significant reduction in size compared with age-matched controls, given that changes in the thalamus can result in central pain (Dunn 2001); (3) changes in central neurotransmitter levels that may alter both autonomic function and sensory afferent input from the gut to the brain; and (4) involvement of the autonomic nervous system. In addition, autonomic dysfunction can contribute to both altered gastrointestinal motility, which may contribute to the gas bloat described in some children, and pain associated with the gut.

Taking all of this information into account can broaden both the suspected potential sources of symptoms and the treatment options. This broad approach can then help the physician decide which medications to select first for an empirical trial, based on safety and the potential for benefit. Medications most commonly suggested for "irritability" in girls who have Rett syndrome include atypical antipsychotics (also known as neuroleptics), such as risperidol, and selective serotonin reuptake inhibitors (SSRIs). The information reviewed here also suggests the potential for benefit from an empirical trial directed at visceral hyperalgesia / central

TABLE 2.2 Specific diagnoses: genetic and metabolic

Rett syndrome

Loss of normal movement and coordination, stereotypic hand movements, seizures, abnormal tone and movement, irritability including crying spells, teeth grinding, breathing irregularities such as rapid breathing (hyperventilation), breath holding and apnea, autonomic dysfunction including irregular heartbeat and prolonged QT interval

Holoprosencephaly

Midline facial anomalies, brain anomalies, seizures, hydrocephalus, hypothalamic dysfunction including hypothermia and altered sleep-wake cycles, endocrine problems including diabetes insipidus (most common), hypothyroidism, glucocorticoid deficiency

Krabbe disease (globoid cell leukodystrophy)

Excessive irritability at presentation, rapid progression over months

GM2 gangliosidosis (Tay-Sachs disease)

Increased startle, myoclonic seizures, spasticity, irritability

Metachromatic leukodystrophy (MLD; infantile and juvenile forms)

Motor and cognitive regression, peripheral neuropathy, visual loss, seizures, gallstones

Pompe disease (glycogen storage disease type II, includes defect in lysosomal metabolism)

Progressive muscle weakness and cardiomyopathy leading to cardiac and respiratory failure, hepatomegaly

Adrenoleukodystrophy (ALD)

Changes in behaviors and learning, seizures, adrenal insufficiency, vision and hearing loss

Menkes disease

Seizures, hypothermia, motor and cognitive regression, irritability

Non-ketotic hyperglycinemia

Severe neonatal coma, seizures, myoclonus, hiccups, apnea; a transient form exists, complicating decision making

neuropathic pain. For this reason, there may be benefit from an empirical trial of gabapentin before trying an atypical antipsychotic, given the better safety profile of gabapentin. An approach to pain treatment is reviewed in greater detail in chapter 4.

Children with Rett syndrome also have a risk for altered cardiopulmonary function as a result of autonomic dysfunction (Rohdin et al. 2007; Weese-Mayer et al. 2008). Identified features include irregular breathing, such as hypoventilation and apnea; abnormal heart rate and heart rhythms; and prolonged QT interval. Heart rate can be evaluated with an electrocardiogram (ECG or EKG). Medications that have a high risk of prolonging the QT interval are reviewed in chapter 3. The cardiorespiratory dysregulation associated with autonomic dysfunction is thought to contribute to the risk for sudden death in Rett syndrome (Rohdin et al. 2007; Weese-Mayer et al. 2008).

Other problems associated with autonomic dysfunction include slow motility of the intestinal tract, which can cause such problems as constipation, gas bloat, and pseudo-obstruction, as reviewed in greater detail in chapter 5 (Malandrini et al. 1998). The problems appear to be a result of autonomic dysfunction in the CNS, rather than dysfunction of the enteric nervous system of the intestines (Deguchi et al. 2000; Deguchi et al. 2001).

One of the challenges with information that is specific to Rett syndrome is the wide range of disability. The information in other chapters may be more relevant to children with severe disability. The intent of reviewing a problem, such as pain, is to indicate the benefit of combining what is known about a specific disease with what is known, in general, about individuals who have impairment of the CNS.

Trisomy 18 and 13

It is initially devastating and overwhelming to learn that your child has trisomy 18 or 13. Equally important, the majority of parents describe the life of their child with trisomy 18 or 13 as meaningful and their child as "happy" (Janvier, Farlow, and Wilfond 2012).

A child with trisomy 18 has identifiable physical features and such CNS malformations as cerebellar hypoplasia, microcephaly, and meningoencephalocele; congenital heart defects, the most common being ventricular septal defect (VSD), patent ductus arteriosus (PDA), and coarctation; intestinal anomalies such as omphalocele and esophageal atresia; and renal anomalies. In studies of children with trisomy 18, 97% were found to have three or more malformations; almost 50% had a congenital heart defect

(Niedrist et al. 2006; Pont et al. 2006). Nearly 40% of children with trisomy 13 have a heart defect (Pont et al. 2006).

Although many children who have trisomy 18 and 13 die in the first month of life, some survive beyond the first year. Survival data for trisomy 18 show that two in three infants survive beyond the first day of life. Studies have found subsequent survival to be 40% to 58% at one week, 22% to 32% at one month, and 3% to 10% at one year (Hsiao et al. 2009; Niedrist et al. 2006; Rasmussen et al. 2003; Vendola et al. 2010). The median survival was 4 to 12 days. Survival data for trisomy 13 are similar, with 58% of babies alive at one week and 3% to 9% at one year, with a median survival of 4 to 7 days (Rasmussen et al. 2003; Vendola et al. 2010; Wyllie et al. 1994). The high early death rate is usually due to central apnea, intermittent lack of breathing resulting from impairment in the area of the brain that controls breathing. Apnea, along with heart defects, contributes to deaths among infants who survive the early days. Children who survive beyond infancy have severe motor and intellectual impairment.

As with many diagnoses, the summary of clinical information focuses on what is "abnormal." What the information does not indicate is that "severe intellectual impairment" does not mean lack of meaningful awareness and response to family. As indicated above, children with trisomy 18 and 13 who survive infancy are viewed by families as having a life of meaning (Janvier, Farlow, and Wilfond 2012).

Deciding whether to perform heart surgery on a child who has trisomy 18 or 13 is difficult, given the short life span of many affected babies and the risk of death unrelated to cardiac defects, most often as a result of central apnea. Studies have revealed that the primary cause of death is most often apnea and that the presence of a heart defect does not seem to affect survival for either trisomy 18 or trisomy 13 (Embleton et al. 1996; Rasmussen et al. 2003; Wyllie et al. 1994).

Studies have begun to investigate the impact of cardiac treatment on the survival of children who have trisomy 18 or 13 (Graham et al. 2004; Kaneko et al. 2008; Kaneko et al. 2009). Two of the studies concluded that children with trisomy 18 or 13 who are treated with palliative or corrective cardiac surgery live longer (Kaneko et al. 2008; Kaneko et al. 2009). One must be careful with these conclusions, because the studies looked at only a small number of affected infants. In addition, the median survival data (the average age of death) in these studies cannot be compared with data from natural history studies, because natural history studies have a high number of deaths in the first day of life. Finally, one study reported that children ventilated for more than two days before surgery were more likely to

remain chronically ventilated after surgery, probably due to central apnea (Graham et al. 2004). Weighing the risk and benefit of medical interventions is covered in detail in chapter 9.

INBORN ERRORS OF METABOLISM

Inborn errors of metabolism (IEMs), also referred to as metabolic diseases, include many disorders that can result in progressive and degenerative damage to the brain. Metabolic disorders, though individually rare, are collectively common. Reports of overall incidence vary by geographic location, with a range of 1 in 784 to 1 in 2,555 live births (Applegarth, Toone, and Lowry 2000; Sanderson et al. 2006).

In general, IEMs interfere with the normal enzymatic or metabolic pathways that are essential to the function of cells in the body. For example, an enzyme facilitates the conversion of a substance into a new product; without the enzyme, this cannot happen. Problems can then arise either due to a build-up of substances that are toxic or that interfere with normal cell function or due to lack of essential compounds that cannot be produced. There are more than five hundred IEMs; only a few of them can be reviewed here. Table 2.1 provides a summary of common symptoms and problems in children with metabolic disorders (Filiano 2006; Levy 2009; Zeviani and Di Donato 2004). Table 2.2 highlights information for a few of the specific diseases.

Treatment intended to alter the outcome of metabolic disorders may involve dietary therapy, stem cell transplantation, enzyme replacement therapy, gene therapy, and liver transplantation. Bone marrow or umbilical cord blood transplantation is considered standard therapy for some diseases, including Hurler syndrome (Boelens et al. 2010). This therapy can also be considered for other diseases before any significant impairment of the brain has occurred, including early or asymptomatic adrenoleukodystrophy (ALD) cerebral form and globoid cell leukodystrophy (GLD). These diseases can be identified before symptoms develop, either through newborn screening or when children without symptoms are tested because a sibling has been diagnosed with the disease. Enzyme replacement therapy (ERT) is standard for some diseases, such as Gaucher disease, and is being investigated for other diseases, including Pompe disease. Clinical trials of ERT and gene therapy for other diseases are underway. Geneticists, metabolic specialists, and pediatric neurologists can assist families with identifying treatment options for specific diseases. Other members of a child's medical care team can help when interventions with unproven benefit are being considered.

A child with a metabolic disorder may have any number of medical problems involving a variety of organ systems, including skeletal abnormalities, enlarged liver, cardiac involvement, and brain abnormalities. Lack of developmental progression, subsequent loss of motor and cognitive skills, and changes in muscle tone are features of many children who have one of these conditions. The brain abnormalities can be divided into those affecting the gray matter (which includes the nerve cells) and those affecting the white matter (the myelinated nerve fibers that conduct electrical impulses away from nerve cells). These classifications help identify what symptoms might be expected, though the involvement in a specific disease may evolve over time to include both gray and white matter.

The gray matter includes regions of the brain involved in muscle control, vision, hearing, memory, emotions, and speech. Diseases that affect the gray matter lead to progressive loss of cognitive abilities, seizures (including myoclonic), and the early onset of dementia. The involvement of the gray matter of the basal ganglia leads to involuntary movement, such as dystonia and chorea (referred to as extrapyramidal signs). Nerve cells of the retina are affected in some disorders, producing pigmentary changes in the retina, referred to as the cherry red spot. Conditions with the features indicated here include some of the lysosomal disorders, such as GM1 gangliosidosis, GM2 gangliosidosis (Tay Sachs), Menkes disease, and some of the mitochondrial disorders, including Leigh syndrome.

White matter is the tissue through which messages pass between different areas of the nervous system. White matter is white because of the fatty substance (myelin) that surrounds the nerve fibers (axons). Diseases of the white matter are often a result of biochemical defects that result in abnormal myelin that breaks down rapidly. Clinically, the earliest sign of most white matter degeneration is abnormal muscle tone. Dementia and seizures can occur, usually much later in the clinical course. Neuropathic pain symptoms also can occur. Visual impairment may be a result of optic atrophy or cortical blindness from demyelination of the optic pathways. Diseases that can involve these findings include metachromatic leukodystrophy (MLD), Canavan disease, and Alexander disease.

NO DIAGNOSIS

Some families face the challenge of having a child who has SNI but does not have a specific diagnosis. This “not knowing” what to expect can be a source of distress. For one thing, these parents do not have the usual ease

of connecting with other families through disease-specific support groups. And there is the added worry of risk with future pregnancies.

Though no information can eliminate these sources of distress, information about the child's condition can still be useful. This situation is similar to that of a child who has cerebral palsy with no identified cause, because CP is a developmental label, not a diagnosis. What the label "SNI" does indicate is the risk for the problems reviewed in this book. Specifically, many of the problems result from CNS impairment. What the label "SNI" also provides is a sense of belonging to a group that can provide support and that understands the experience of caring for a child who has SNI.

For these children, the risk to health becomes identified as each problem is identified. Similarly, some diagnoses have a variable outcome that becomes clear as the child's journey unfolds. While no crystal ball exists to map out any child's future, a specific diagnosis means having more information about possible future scenarios. For all parents of a child who has SNI, there is a balance of hoping for the best while anticipating the problems that are possible. This is not an easy journey. The physician hopes to provide information to assist with this balance. One parent identified the perspective of having a child with no specific diagnosis and therefore no information on the long-term outcome thus: "we have been blessed that no one can put her life and its future in a box. They can't tell me what typically can or cannot happen, they cannot tell me she will never be able to accomplish something" (Moeykens 2011).

AREAS OF THE CNS THAT CAN BE AFFECTED IN SNI

The following general summary of brain structures helps explain why children who have SNI can have many of the problems reviewed in this book (figure 2.1).

The cerebral hemispheres are the two halves of the cerebrum, connected to each other by the corpus callosum. The cerebrum is further divided into the frontal, parietal, temporal, and occipital lobes. The functions of the cerebral hemispheres include consciousness (awareness of one's self and one's environment), thinking, reasoning, memory, language, speech, vision, hearing, touch, motor control, and emotions.

The thalamus is a midline, paired, symmetric structure located between the cerebral cortex and the midbrain. It receives and processes sensory signals from the body (somatic), and from the intestinal tract and bladder (visceral). It is also involved in regulating states of sleep and arousal (alertness).

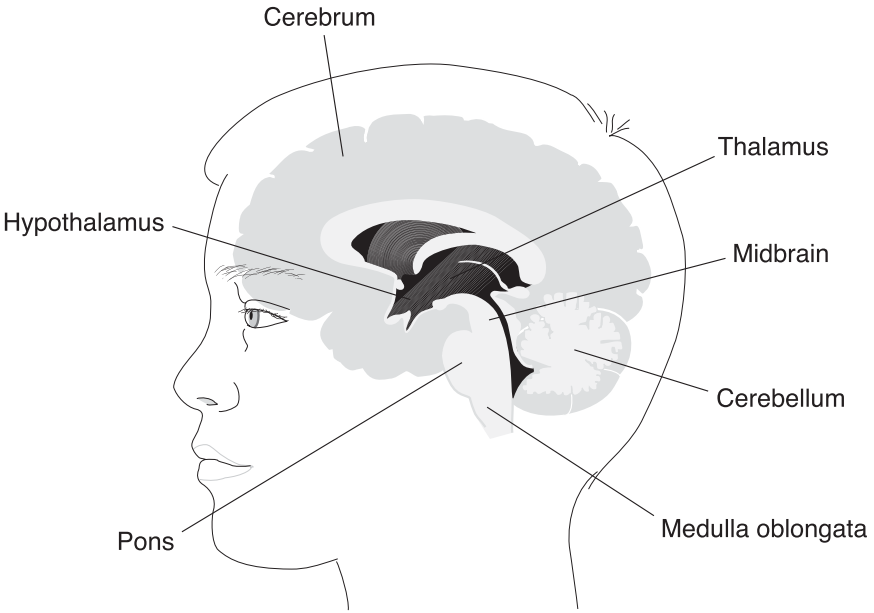


Figure 2.1. Midsection view of the brain.

The basal ganglia are a group of nerve cells (nuclei) that are strongly connected to the cerebral cortex, thalamus, and other areas of the CNS. Functions include voluntary control of movement.

The hypothalamus is located in the midline, below the thalamus. It links the nervous system to the endocrine system via the pituitary gland. In addition, it is involved in the regulation of the autonomic nervous system. Functions that are controlled by the hypothalamus include heart rate, blood pressure, body temperature, and sleep. Endocrine function that is linked to the hypothalamus includes thyroid function, water and sodium regulation, steroid release, and pubertal development.

The midbrain is located between the thalamus/hypothalamus and the brain stem. It is involved in the regulation of vision, hearing, motor control, sleep-wake cycles, arousal (alertness), and temperature.

The pons is located in the brain stem, between the midbrain and the medulla. It is involved in the regulation of sleep, breathing, swallowing, bladder control, eye movement, facial expressions, and the secretion of saliva and tears.

The medulla is located below the pons. The medulla contains the respiratory, vomiting, cardiac, and vasomotor centers involved in autonomic

regulation, which helps regulate breathing, heart rate, blood pressure, swallowing, and vomiting.

A SMALL WINDOW INTO THE FUTURE: PROGNOSIS AND LIFE EXPECTANCY

Prognosis is defined as a prediction of the probable course and outcome of a disease. *Prognosis* is also used to indicate the likelihood of recovery from an illness, such as the likelihood of recovering from pneumonia. For children who have SNI, there are two parts to prognosis: the developmental outcome and the medical outcome. They are related yet distinctly different. They are related in that many of the medical problems are a result of CNS impairment that also inhibits neurological development. Yet the timing of when medical problems arise is variable for children with similar levels of neurological impairment.

Confusion arises when the two outcomes are not looked at separately. It can be helpful to review what is known and anticipated about the neurological outcome separately from what is known and anticipated about the health outcome. In general, the neurological outcome is more predictable and the health outcome more variable. In anticipating the neurological outcome, some parents may be told that their child "won't do anything." This is often inaccurate, as most children acquire a meaningful response to their environment and can communicate through facial expression and vocalization. A more accurate statement is likely to be that the child "will remain dependent on others for care and will not acquire language skills of communication." Neither of these statements predicts when problems in health will occur, however. To put it simply, medical problems arise when a problem that can compromise health arises.

Information is available about life expectancy for the developmental label "cerebral palsy" and for specific diagnoses. In general, such information is of limited benefit as it is a snapshot of many children that is difficult to apply to an individual child. In addition, the data are often outdated, not reflecting how life expectancy is altered by changes in how care is provided.

The information in this chapter provides a general review of what is known about common problems seen in children with SNI, recognizing that parents often wonder and worry, "What will happen?" "How long will my daughter live?" and "When will we know?" The most important guide will always be the child's story. Throughout this book, I review problems to anticipate and problems that exist and provide a framework to

reflect on the story as decisions are faced. The later part of the journey is covered in detail in chapter 9.

Static impairment

Information about life expectancy for children who have CP demonstrates a wide variation. The more severe the motor disability, the more likely it is that a child will not survive into adulthood. An example of severe motor disability would be the child's inability to lift up the head when lying on his or her stomach. In one review, survival for individuals who have CP with "global" impairment in vision, hearing, intellect, and motor functions, as indicated by being dependent on others for mobility and feeding, was 50% at 13 years and 25% at 30 years (Hutton and Pharoah 2006). Recurrent respiratory illness leading to respiratory failure is the most common cause of mortality in children who have severe CP (Hemming, Hutton, and Pharoah 2006; Katz 2003; Strauss, Cable, and Shavelle 1999). Information about CP is relevant to any disease with CNS dysfunction that results in severe impairment of muscle tone and coordination of muscle movement.

The information from these and other studies, however, is about children born more than 15 years ago. Why are the studies so old? Because time is needed to follow a group of children, and then more time is needed to analyze the data and submit for publication. Survival is probably much longer for children born since 2000, because care options have expanded in the past 15 years. For example, interventions to assist with the clearance of mucus from the lungs are now routine, including use of the pulmonary vest and cough assist device. These were first used in conditions such as cystic fibrosis and Duchenne muscular dystrophy. Starting in the late 1990s, their use was expanded to children who have CP and similar conditions. The aggressive attention to mucus clearance, along with the use of antibiotics and steroids, has probably expanded survival by years, possibly by decades.

Some congenital conditions are described as having survival with two phases, with early death in those who have the most severe impairment. As an example, a review of survival of children with hydranencephaly found an average life expectancy of 7.7 years, with steeper mortality in the first two years and a more gradual decline for those who survived beyond the first two years (Merker 2008). This pattern was also identified with children who have alobar holoprosencephaly (HPE), the most severe form of HPE. Though most deaths occurred within the first days to weeks of

life, those infants who survived the first month were likely to survive beyond infancy (Whiteford and Tolmie 1996). This is similar to the information provided for trisomy 18 and 13, as reviewed earlier.

These findings seem to indicate that survival early in life is determined by the presence or absence of central apnea. Other factors include severe impairment that compromises breathing early in life, such as severe hypotonia and the absence of a cough and gag response. For children without these problems early in life, health problems can be anticipated and managed as they arise. Compromise to health is then a much more gradual process, often occurring over years. Such health problems are often related to the motor disability, regardless of the cause, such as oral motor dysfunction and recurrent pulmonary aspiration.

Another consideration is the risk of sudden, unexpected death, a much less common cause of mortality. This is clearly a distressing matter. How does a parent anticipate or plan for the unexpected? The goal is to be informed, but to manage information so that it is not a predominant focus of thought. Risk factors for sudden death include central disordered regulation of breathing and intractable epilepsy. One of the risks associated with epilepsy is sudden unexpected death in epilepsy (SUDEP), though this is an infrequent occurrence and is less common in children than in adults (Tomson, Nashef, and Ryvlin 2008).

A final consideration is the higher risk of mortality associated with life-threatening episodes of intestinal pseudo-obstruction. It is unclear whether surgery provides a better outcome than conservative management. This specific problem is also covered in chapter 5.

The label "vegetative state"

Neurology has developed categories to indicate different levels of consciousness. These include the label "vegetative state," defined by three main clinical features: (1) cycles of eye opening and closing, giving the appearance of sleep-wake cycles; (2) complete lack of awareness of the self or the environment; and (3) complete or partial preservation of hypothalamic and brain stem autonomic functions (Monti, Laureys, and Owen 2010). Other individuals may show partial and fluctuating awareness, called a "minimally conscious state," in which there is inconsistent but reproducible purposeful behavior.

The Multi-Society Task Force on PVS (1994), consisting of U.S. adult and pediatric neurologists and neurosurgeons, summarized extensive outcome data on this condition (referred to as *persistent* vegetative state). It

concluded that the condition could be declared *permanent* 3 months after nontraumatic injury (resulting from lack of oxygen) and 12 months after traumatic brain injury in children. In the review, of the children in a vegetative state one month after traumatic injury, 9% were dead at one year post injury, 27% were independent with good recovery to moderate disability, and the rest were in a vegetative or minimally conscious state. For those with nontraumatic CNS injury, 22% had died by one year, and of the 13% who acquired consciousness (most within the first 3 months), 6% were independent at one year and the other 7% had severe disability.

The label "PVS" has unintended consequences, including physicians focusing on the need for a family to "accept" the diagnosis before they have had a chance to fully understand this new reality for their child. As with many labels, there is benefit to be gained in that the label provides a context for how we can best understand a child's condition. Yet there is harm when it creates an expectation that a family "needs" to accept the information and an assumption about what they "should" do with the information. This is a time when a family needs "space" and time to understand the new reality as they develop an understanding of what has changed for their child. Many of the principles outlined in chapter 9 are intended to assist families with this process of "relearning" their child, including identifying hopes, fears, and ultimate goals for the child, that can serve as a guide to decisions.

Lauren is a 3-year-old who has SNI caused by a near-drowning event 5 months ago, resulting in severe anoxic injury to the brain. The neurologist believes she is in a PVS. Her mother observes a consistent response from Lauren to her voice. She remains hopeful that Lauren will continue to improve. The medical team is concerned that she has "unrealistic expectations" for her daughter. Lauren's father does not observe any response from his daughter. He wishes to be hopeful, but does not anticipate any improvement in his daughter. At a meeting with both parents, Lauren's father asks, "Is there any hope that she will walk or talk? I want to believe that her mother sees what she describes, but I'm not sure which one of us is right."

The chronic care specialist and palliative care team validate the experience of Lauren's parents. This is framed as "you both have an ongoing relationship with your daughter and both observations are valid, as she is defined by her relationships with her family, and the goals that you have identified for your daughter." In answer to the question "Will she walk or talk?" the parents are given permission to maintain their hope. The medical information is presented as follows: "We have the same hopes for Lauren. We also have a responsibility

to her and to you to give you honest answers with the best medical information we have. Following a severe lack of oxygen to the brain, after more than 3 months, it is not expected to see further recovery of the function of the brain. This specifically means that she will remain dependent on you and others for all of her physical care and will remain dependent on you for all decision making on her behalf throughout her life. Lauren will not gain the ability to walk independently or to communicate with words. It sounds like you have identified how she is able to communicate with some facial expression. We are glad that Lauren's discomfort is reasonably managed with current medications, given your goal that she remains comfortable. We believe it is important that you are viewed and supported as having the best understanding of what Lauren experiences and what her days are like. We wish to continue to work together on how Lauren's medical care can meet your goals for Lauren. We will continue to identify what can enhance her life and discuss in an honest manner what may not allow that to happen. As we follow with you on this journey, we will monitor for changes in her comfort, review periodically if your goals for Lauren have changed as we have discussed previously, and adjust her care plan as needed." The parents are asked whether they have questions about the information presented by the neurologist, including spinal reflex (a response to a stimulus, resulting in movement that is under the control of the spinal cord without involvement of the brain). They reply, "We feel like we understand what they are telling us." During this conversation, Lauren's mother shares, "I know she probably won't get better, but I need to have hope. I don't want others to give up on her while we figure out what is best for her."

Lauren develops increasing discomfort, noted as episodes with increased heart rate, sweating, facial flushing, an anxious look on her face, moaning, back arching, and stiffening of her limbs. A combination of medications decreases the frequency and severity of these episodes, initially by 75%. As episodes worsen again, it is difficult to improve her comfort sufficiently without excessive sedation. Her parents redirect their decisions to focus on improving Lauren's comfort rather than treating new illnesses that arise. They feel it is more appropriate for Lauren to be sedated, if needed, to be comfortable: "She can't enjoy much when she is awake anyway, she just looks so miserable." Lauren's mother is grateful for the time and guidance that allowed her to better understand her daughter's needs and problems. "I just needed to know that I gave her a chance. I think she is telling us what she needs, and it isn't to live longer with medical treatment but to be as comfortable as possible for the remainder of her time with us."

Metabolic diseases

One must be very cautious about the information available for life expectancy for each metabolic disease. Each disorder is rare, and with the improvements in care, especially respiratory care, over the past decade, published information is often outdated. To illustrate, one website indicates that "even with the best of care, children with Tay-Sachs disease usually die by age 4" (NINDS 2011). Yet in a recent retrospective natural history study, 25% of children were alive at 5 years of age (Bley et al. 2011).

The important point is to use information as a guide, not as a predictor. The child's story is the best guide. Ultimately, focusing on what parents identify as the goals for their child and allowing these goals to guide decisions will be more relevant for each child.

References

Applegarth DA, Toone JR, Lowry RB. 2000. Incidence of inborn errors of metabolism in British Columbia, 1969–1996. *Pediatrics* 105(1):e10.

Bley AE, Giannikopoulos OA, Hayden D, et al. 2011. Natural history of infantile G(M2) gangliosidosis. *Pediatrics* 128(5):e1233–41.

Boelens JJ, Prasad VK, Tolar J, et al. 2010. Current international perspectives on hematopoietic stem cell transplantation for inherited metabolic disorders. *Pediatr Clin North Am* 57(1):123–45.

Deguchi K, Antalffy BA, Twohill LJ, et al. 2000. Substance P immunoreactivity in Rett syndrome. *Pediatr Neurol* 22(4):259–66.

Deguchi K, Reyes C, Chakraborty S, et al. 2001. Substance P immunoreactivity in the enteric nervous system in Rett syndrome. *Brain Dev* 23(Suppl 1):S127–32.

Downs J, Géranton SM, Bebbington A, et al. 2010. Linking MECP2 and pain sensitivity: the example of Rett syndrome. *Am J Med Genet A* 152A(5):1197–205.

Dunn HG. 2001. Neurons and neuronal systems involved in the pathophysiologies of Rett syndrome. *Brain Dev* 23(Suppl 1):S99–100.

Embleton ND, Wyllie JP, Wright MJ, et al. 1996. Natural history of trisomy 18. *Arch Dis Child Fetal Neonatal Ed* 75(1):F38–41.

Filiano JJ. 2006. Neurometabolic diseases in the newborn. *Clin Perinatol* 33(2):411–79.

Graham EM, Bradley SM, Shirali GS, et al. 2004. Effectiveness of cardiac surgery in trisomies 13 and 18 (from the Pediatric Cardiac Care Consortium). *Am J Cardiol* 93(6): 801–3.

Hemming K, Hutton JL, Pharoah PO. 2006. Long-term survival for a cohort of adults with cerebral palsy. *Dev Med Child Neurol* 48(2):90–95.

Hotchkiss RS, Strasser A, McDunn JE, Swanson PE. 2009. Cell death. *N Engl J Med* 361(16): 1570–83.

Hsiao CC, Tsao LY, Chen HN, et al. 2009. Changing clinical presentations and survival pattern in trisomy 18. *Pediatr Neonatol* 50(4):147–51.

Hutton JL, Pharoah PO. 2006. Life expectancy in severe cerebral palsy. *Arch Dis Child* 91(3): 254–58.

International Hydranencephaly Support Group. No date. Hydranencephaly frequently asked questions. http://hydranencephaly.com/Brochures/Hydranfaq.pdf. (accessed May 23, 2010).

IRSF (International Rett Syndrome Foundation). 2011. Testing & diagnosis. www.rettsyndrome.org/content/blogcategory/133/971.

Janvier A, Farlow B, Wilfond B. 2012. The experience of families with children with trisomy 13 and 18 in social networks. *Pediatrics* 130(2):293–98.

Kaneko Y, Kobayashi J, Achiwa I, et al. 2009. Cardiac surgery in patients with trisomy 18. *Pediatr Cardiol* 30(6):729–34.

Kaneko Y, Kobayashi J, Yamamoto Y, et al. 2008. Intensive cardiac management in patients with trisomy 13 or trisomy 18. *Am J Med Genet A* 146A(11):1372–80.

Katz RT. 2003. Life expectancy for children with cerebral palsy and mental retardation: implications for life care planning. *NeuroRehabilitation* 18(3):261–70.

Levy PA. 2009. Inborn errors of metabolism, part 2: specific disorders. 2009. *Pediatr Rev* 30(4):e22–28.

Malandrini A, Hayek G, Villanova M, et al. 1998. Ultrastructural study of enteric ganglia in three patients with Rett syndrome. *Brain Dev* 20(8):586–88.

Merker B. 2008. Life expectancy in hydranencephaly. *Clin Neurol Neurosurg* 110(3):213–14.

Moeykens S. 2011. One family's genetics journey. *Complex Child E-Magazine.* http://articles.complexchild.com/dec2011/00348.html.

Monti MM, Laureys S, Owen AM. 2010. The vegetative state. *BMJ* 341:292–96.

Multi-Society Task Force on PVS. 1994. Medical aspects of the persistent vegetative state (part 2). *N Engl J Med* 330(22):1572–79.

Neul JL, Kaufmann WE, Glaze DG, et al., RettSearch Consortium. 2010. Rett syndrome: revised diagnostic criteria and nomenclature. *Ann Neurol* 68(6):944–50.

Niedrist D, Riegel M, Achermann J, Schinzel A. 2006. Survival with trisomy 18—data from Switzerland. *Am J Med Genet A* 140(9):952–59.

NINDS (National Institute of Neurological Disorders and Stroke). 2011. Tay-Sachs disease information page. www.ninds.nih.gov/disorders/taysachs/taysachs.htm.

Percy AK, Lane JB. 2005. Rett syndrome: model of neurodevelopmental disorders. *J Child Neurol* 20(9):718–21.

Pont SJ, Robbins JM, Bird TM, et al. 2006. Congenital malformations among liveborn infants with trisomies 18 and 13. *Am J Med Genet A* 140(16):1749–56.

Rasmussen SA, Wong LY, Yang Q, et al. 2003. Population-based analyses of mortality in trisomy 13 and trisomy 18. *Pediatrics* 111(4 Pt 1):777–84.

Rays of Sunshine. No date. What if? Part 1: Your child's last days. www.hydranencephaly.com/whatifpt1childslastdays.htm (accessed March 31, 2011).

Rohdin M, Fernell E, Eriksson M, et al. 2007. Disturbances in cardiorespiratory function during day and night in Rett syndrome. *Pediatr Neurol* 37(5):338–44.

Sanderson S, Green A, Preece MA, Burton H. 2006. The incidence of inherited metabolic disorders in the West Midlands, UK. *Arch Dis Child* 91(11):896–99.

Strauss D, Cable W, Shavelle R. 1999. Causes of excess mortality in cerebral palsy. *Dev Med Child Neurol* 41(9):580–85.

Tomson T, Nashef L, Ryvlin P. 2008. Sudden unexpected death in epilepsy: current knowledge and future directions. *Lancet Neurol* 7(11):1021–31.

Vendola C, Canfield M, Daiger SP, et al. 2010. Survival of Texas infants born with trisomies 21, 18, and 13. *Am J Med Genet A* 152A(2):360–66.

Weese-Mayer DE, Lieske SP, Boothby CM, et al. 2008. Autonomic dysregulation in young girls with Rett syndrome during nighttime in-home recordings. *Pediatr Pulmonol* 43(11):1045–60.

Whiteford ML, Tolmie JL. 1996. Holoprosencephaly in the west of Scotland 1975–1994. *J Med Genet* 33(7):578–84.

Wyllie JP, Wright MJ, Burn J, Hunter S. 1994. Natural history of trisomy 13. *Arch Dis Child* 71(4):343–45.

Zeviani M, Di Donato S. 2004. Mitochondrial disorders. *Brain* 127(Pt 10):2153–72.

CHAPTER 3

Treating Pain and Other Distressing Symptoms
An Overview

We must learn to regard people less in the light of what they do or omit to do, and more in the light of what they suffer.
—Dietrich Bonhoeffer

Children and adults with severe neurological impairment often experience problems that cause pain and discomfort. They experience other distressing symptoms as well, such as retching and vomiting, excessive respiratory secretions, shortness of breath, and impaired sleep. And there are also problems associated with the impairment of the central nervous system, such as muscle spasms, dystonia, and autonomic dysfunction.

Unfortunately, these distressing symptoms often are not treated in children who have SNI. One study found that more than 90% of children who had cerebral palsy and pain had experienced pain for more than a year—yet only half of them were receiving any pain treatment at all (Svedberg et al. 2008). One reason for the lack of treatment is that physicians often find it challenging to identify the cause of pain in a nonverbal child who has SNI. Another is that physicians may not be aware of the range of treatment options that can improve comfort for these children. Finally, the use of medications to improve comfort may make parents feel they must choose between maintaining their child's health and improving their child's comfort.

The goal of this chapter is to provide an overview of these significant challenges and to review how pain is identified in nonverbal children who have SNI. Details about the medical evaluation and management of each problem, along with strategies for symptom treatment, are provided in chapters 4 through 7.

IDENTIFYING PAIN IN THE NONVERBAL CHILD WHO HAS SNI

Answering the question "Is it pain?" is clearly complicated when considering nonverbal children who have SNI. Many parents worry about the difficulty of recognizing their child's pain. They ask, "How will I know if what I am seeing in my child is pain?" and "What if my child is in pain but can't show me?" Adding to this challenge, many of the features associated with pain in such children can also be a result of the brain impairment. Fortunately, much has been learned in the past ten years to help guide pain assessment in nonverbal children with SNI.

Features that indicate pain

Nonverbal children and adults with impairment of the CNS have specific features, referred to as pain behaviors, that are observed when they experience pain. These behaviors have been identified in studies of people with CNS impairment after they have had surgery and after other painful procedures, when they are likely to be experiencing pain, as well as by asking parents and caregivers what they observe when they believe a child is in pain. Similar behaviors are consistently associated with pain in children and adults who have SNI:

- Crying and moaning
- Changes in facial expression, including grimacing and frowning; a distressed look
- Inability to be consoled and made comfortable
- Changes in the level of interaction, such as becoming withdrawn
- Changes in the amount of movement, such as an increase in movement of the arms and legs
- Becoming restless and fidgety
- Changes in muscle tone and the position of the body, including arching of the back and stiffer muscles
- Increased heart rate and sweating

In addition to these common pain behaviors, some children display atypical behaviors such as laughing, lack of facial expression, or self-injurious behavior (Breau, McGrath, et al. 2002; Hadden and von Baeyer

2002; Malviya et al. 2006; Stallard et al. 2002). Children who display atypical pain behaviors are especially vulnerable to not having their pain identified. Some physicians lack the knowledge that such behaviors may indicate pain.

The studies that identified these pain behaviors also concluded that each child displays a unique set of behaviors. From these studies, we also know that parents rate themselves as accurate at identifying pain in their child, but they consider pain identification to be an uncertain and complex process (Carter, McArthur, and Cunliffe 2002; Stallard et al. 2002). Uncertainty about pain is increased if, when a parent shares concerns about the child's pain, the healthcare provider is unfamiliar with the range of behaviors associated with pain. In one study, parents felt they would be unable to describe what they considered to indicate pain in their child, yet they quickly identified the pain behaviors their child exhibited when they were given a list of such behaviors known to occur in nonverbal children who have SNI (Breau et al. 2000). Parents who have detailed information about pain assessment are empowered to become experts in the assessment of pain in their child.

Pain assessment tools

There are tools for assessing pain behaviors in nonverbal children who have SNI. These tools can translate the expertise of parents into information that can be communicated to others. Because pain assessment in such children has been studied mostly in the past ten years, many physicians are not yet familiar with all of the possible pain behaviors. Pain assessment tools can help empower parents in recognizing specific pain behaviors in their child, and parents can share this information with their child's healthcare providers when necessary. The information provided in a pain assessment tool can prevent the situation in which, when a parent shares his or her concerns about a child's pain, a physician inaccurately reassures the parent that the child is not in pain, especially likely when the pain behaviors are atypical.

Each of the pain assessment tools available for children who have SNI has different advantages. The ultimate goal always is to provide the simplest yet most accurate picture for each child. The pain assessment tools can assist in several ways:

- Inform parents and healthcare providers about the types of behaviors associated with pain in children who have SNI

- Empower parents by documenting behaviors that indicate pain in their child, giving them a legitimate voice in different care settings
- Empower parents whose child displays atypical behaviors such as laughing, withdrawal, or blunted facial expression, behaviors that in the past have made such children especially likely not to receive appropriate identification and treatment of their pain
- Assess for the presence of pain in the moment, such as following surgery and painful procedures, by determining whether the pain score reaches a minimum threshold
- Assist with monitoring for the benefit of a new medication by assessing severity before and after the new intervention to treat pain
- Assess for the presence of "breakthrough" pain in a child receiving chronic treatment, allowing intermittent use of medications with quick onset to treat acute symptoms

The pain assessment tools for nonverbal children with neurological impairment are summarized in table 3.1. A few comments about the Revised-Face, Legs, Activity, Cry, Consolability (R-FLACC) scale and the Individualized Numeric Rating Scale (INRS) are warranted, because these scales were designed to be individualized by indicating behaviors specific to each child, with examples provided. This ability to add specific behaviors is an important feature for children with atypical pain behaviors that are not present in the other tools. No one tool is ideal for all children. On the one hand, the R-FLACC includes a greater variety of behaviors (table 3.2). This can be an advantage when learning the types of behaviors associated with pain in nonverbal children who have SNI. On the other hand, if a child becomes withdrawn with severe pain, the INRS can be individualized to indicate the appropriate pain rating (figure 3.1). In such a child who has few other pain behaviors, ratings on other pain tools, including the R-FLACC, will be falsely low. (An example of an individualized R-FLACC is provided in table 3.3.)

Pain also results in physiological changes; that is, changes in the normal functions of the body. Changes associated with pain include sweating, pale skin, and an increase in heart rate and blood pressure. These occur most commonly with acute pain, such as with an invasive procedure or surgery. These changes are not as reliable in assessing chronic pain, including that in children who have SNI (Hunt et al. 2007; Oberlander et al. 1999). Heart rate, blood pressure, sweating, and changes in skin color can be affected by autonomic dysfunction, another problem that can occur in

TABLE 3.1 Pain assessment tools for nonverbal children with neurological impairment

Revised-Face, Legs, Activity, Cry, Consolability (revised-FLACC)

- Revised from the FLACC to include pain behaviors specific to children with cognitive impairment (Malviya et al. 2006)
- Like the FLACC, a five-item pain assessment tool with a score ranging from 0 to 10
- Allows parents to individualize by adding behaviors specific to their child (examples provided)
- Option of indicating individualized behaviors can be beneficial for children with unusual pain behaviors and lack of other typical features, which may result in a false low score on other tools

Individualized Numeric Rating Scale (INRS)

- A personalized pain assessment tool for nonverbal children with intellectual disability, based on the parent's knowledge of the child, developed for use in the hospital (Solodiuk et al. 2010)
- A parent identifies behaviors that indicate no pain to the worst possible pain, on a scale ranging from 0 to 10
- Moderate to strong correlation between INRS ratings and NCCPC-PV (see below) total scores
- Option of indicating individualized behaviors can be beneficial for children with unusual pain behaviors and lack of other typical features, which may result in a false low score on other tools

The Non-Communicating Children's Pain Checklist-Postoperative Version (NCCPC-PV)

- A 27-item pain assessment tool for children with severe cognitive impairment (Breau, Finley, et al. 2002)
- Moderate to severe pain determined at a cut-off of 11 or more out of 81
- In Breau, Finley, et al. 2002, this cut-off provided a sensitivity of 0.88 and specificity of 0.81, indicating that a child with a score of 11 or more was accurate at indicating pain 88% of the time, and a score of 10 or less was accurate at indicating no pain 81% of the time

The Non-Communicating Children's Pain Checklist-Revised (NCCPC-R)

- A 30-item pain assessment tool for children with severe cognitive impairment (Breau, McGrath, et al. 2002)
- Moderate to severe pain determined at a cut-off of 7 or more out of 90
- In Breau, McGrath, et al. 2002, this cut-off provided a sensitivity of 0.84 and specificity of 0.77
- Revised from the NCCPC-PV (postoperative version)

TABLE 3.1 *(continued)*

Paediatric Pain Profile (PPP)

- A 20-item pain assessment tool for children with severe to profound cognitive impairment (Hunt, Goldman, et al. 2004)
- Scores of 14 or more were generally associated, by observers, with moderate or severe pain
- A cut-off of 14 provided a sensitivity of 1.0 and specificity of 0.91
- The tool is arranged to provide different scores to indicate a rating for "On a good day," "Most troublesome pain," "Second most troublesome pain," etc.
- Available to download from the web, following registration, at www.ppprofile.org.uk

these children. Physiological measures may have a role in monitoring pain when used to supplement other, more reliable information.

Identifying a score from a pain assessment tool is beneficial, but it is also important to not become overly dependent on numbers. Another consideration is that assessment tools are not available for other distressing symptoms in nonverbal children. It is beneficial to estimate the frequency and duration of such distressing symptoms. The following information will help with assessing the benefit of a medication for symptom treatment:

- Have the features indicating the symptom or problem improved? Examples:
  - — Crying, grimacing, spasms, and arching associated with pain
  - — Flushing (redness of skin), sweating, increased secretions, agitation, and stiffening with autonomic dysfunction
  - — Agitation and distressed look with dyspnea
- Has the severity of the symptom improved? Have the frequency and duration of the episodes decreased?
  - — How much improvement in the severity of the symptom would you estimate? Is your child 25% improved, 50% improved, greater than 50% improved, mostly resolved?
  - — How often are distressing episodes now occurring? What is the duration of a typical episode and of the longest episode?

Emily is a 7-year-old who has a genetic disorder, associated motor and intellectual impairment, gastroesophageal reflux, and bowel dysmotility. Her mother is concerned about her daughter's comfort but is not certain whether Emily is in pain. When asked to describe how her daughter looks and acts

TABLE 3.2 Revised-Face, Legs, Activity, Cry, Consolability (R-FLACC)

Category	0	1	2	Individualized behaviors*
Face	No particular expression or smile _____	Occasional grimace or frown; withdrawn or uninterested; appears sad or worried _____	Consistent grimace or frown; frequent/constant quivering chin, clenched jaw; distressed-looking face; expression of fright or panic; other (write in): _____	Examples: "Pouty" lip; clenched and grinding teeth; eyebrows furrowed; stressed looking; stern face; eyes wide open, looks surprised; blank expression; nonexpressive
Legs	Normal position or relaxed; usual tone and motion to limbs _____	Uneasy, restless, tense; occasional tremors _____	Kicking, or legs drawn up; marked increase in spasticity, constant tremors or jerking; other (write in): _____	Legs and arms drawn to center of body; clonus in left leg with pain; very tense and still; legs tremble
Activity	Lying quietly, normal position, moves easily; regular, rhythmic respirations _____	Squirming, shifting back and forth, tense or guarded movements; mildly agitated (e.g., head back and forth, aggression); shallow, splinting respirations, intermittent sighs _____	Arched, rigid or jerking; severe agitation; head banging; shivering (not rigors); breath holding, gasping, or sharp intake of breaths, severe splinting; other (write in): _____	Grabs at site of pain; nods head; clenches fists, draws up arms; arches neck; arms startle; turns side to side; head shaking; points to where it hurts; clenches fist to face, hits self, slapping; tense, guarded, posturing; thrashes arms; bites palm of hand; holds breath

Cry	No cry or verbalizing _____	Moans or whimpers; occasional complaint; occasional verbal outburst or grunt _____	Crying steadily, screams or sobs, frequent complaints; repeated outbursts, constant grunting; other (write in): _____	Mouth wide open and screaming; gasping, screaming; grunts or short responses; whining, whimpering, wailing, shouting; crying is rare
Consolability	Content and relaxed _____	Reassured by occasional touching, hugging, or being talked to; distractible _____	Difficult to console or comfort; pushing away caregiver, resisting care or comfort measures; other (write in): _____	Responds to cuddling, holding, parent, stroking, kissing; distant and unresponsive when in pain

Note: Guidelines: (1) review to identify behaviors and features that are associated with pain in your child; (2) add behaviors not listed, using examples as needed; (3) use to indicate to others the child's pain behaviors and to document total pain score as needed.

*Examples of additional pain behaviors identified by parents in the study by Malviya et al. (2006).

Directions:

1. Think about your child's past painful events. How does your child act when in mild pain, moderate pain, or severe pain?

2. In the diagram below, write in your child's typical pain behaviors on the line that corresponds to pain intensity, where 0 = no pain and 10 = worst possible pain.

3. When describing your child's pain, think about changes in:
   a. Facial expression: Squinting eyes, frowning, distorted face, grinds teeth, thrusts tongue
   b. Leg or general body movements: Tense, gestures or touches part of body that hurts
   c. Activity, or social interaction: Not cooperative, cranky, irritable, unhappy; not moving, quiet or less active, more active, fidgety
   d. Cry or vocalization: Moaning, whimpering, crying, yelling
   e. Consolability: Less interactive, seeks comfort or physical closeness, difficult to distract/satisfy
   f. Other changes: Tears, sweating, holds breath, gasping

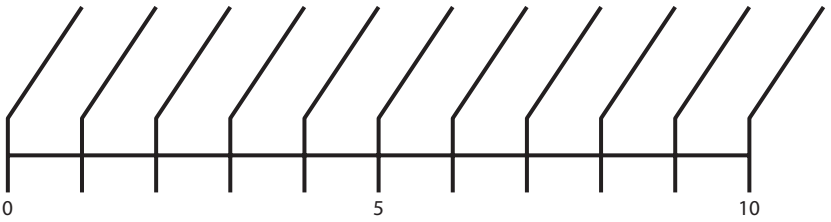


Figure 3.1. Individualized Numeric Rating Scale (INRS). *Adapted and used with permission from J. Solodiuk and M. A. Curley, "Pain Assessment in Nonverbal Children with Severe Cognitive Impairments: The Individualized Numeric Rating Scale (INRS),"* J. Pediatr. Nurs. *18, no. 4 (2003): 295–99, p. 297.*

when she is thought to be in pain, she shares, "I know it will sound weird, but she gets quiet, clingy, and laughs, but it isn't a happy laugh."

Emily's mother is relieved to understand that some children with SNI will display these features when in pain. The R-FLACC is used to develop an individualized pain assessment tool that can be used in the hospital and with Emily's home nurses. This tool is of great assistance when making decisions about when to use an as-needed (prn) pain medication. Tramadol is used as needed, with benefit for Emily—greatly improving her daily comfort. The pain assessment tool is also beneficial when working with the specialists involved in Emily's care, facilitating integration of a chronic pain management plan with a daily scheduled medication for possible visceral hyperalgesia into the medical management of her gastrointestinal problems.

Emily's individualized R-FLACC is summarized in table 3.3.

Determining whether pain behaviors indicate pain

The tools described above have been available only for the past decade. Most physicians have not been trained in the assessment and treatment of

TABLE 3.3 Emily's individualized R-FLACC

Category	0	1	2
Face	No particular expression or smile	Withdrawn	Distressed-looking face, teeth grinding
Legs	Normal position or relaxed, usual tone and motion to limbs	Occasional tremors	Constant tremors
Activity	Lying quietly, normal position, moves easily, regular and rhythmic respiration	Squirming, withdrawn, decrease in sleep	Shivering, breath holding, gasping, withdrawal, seeking physical closeness, sweating
Cry	No cry	Moans or whimpers	Soft cry, frequent laughing without smile
Consolability	Content, relaxed	Reassured by occasional touching	Difficult to console or comfort

pain in children who have SNI. These tools can be helpful if a parent encounters a clinician who does not think the child's behaviors indicate pain. Even more beneficial is to focus away from the question "Is it pain?" and instead determine whether pain is one of the sources that could explain the observed behaviors. This helps avoid the need to know with "certainty" before initiating treatment for pain. Occasionally, a physician may say that some children with SNI cannot feel pain, because of the severity of brain damage. This should never be considered a valid assessment. Instead, the risk of untreated pain should be considered far greater than the risk of a pain treatment trial for observed behaviors that are not a result of pain. Improvement following such a medication trial suggests pain, such as from one of the neuropathic pain sources. Chapter 4 reviews the sources of pain to consider in children with SNI, along with the treatment options.

Another reason children who have SNI are at risk for under-recognition of pain and distress is a tendency to see potential pain behavior as "this is what she does," often with an explanation identified for the observed behaviors. We can become immune to the features that suggest pain—such

as stiffening of extremities, back arching, and restlessness—given how frequently they occur in these children. It helps to ask at such times, Is there room for improvement in comfort even if there is a problem that is considered to be the source of the discomfort? The case of George at the end of chapter 4 illustrates this point: a pain treatment plan significantly improved his comfort, though his symptoms were previously explained by various problems. Parents can also feel responsible for their child's comfort, spending hours a day using comfort measures such as venting the gastrostomy tube or holding and rocking the child. Such extraordinary efforts are an indirect indicator of discomfort that can benefit from a pain treatment plan.

By increasing awareness of the features that suggest pain and the approach to evaluating and managing pain, the gap between parent and physician will close—as physicians become more knowledgeable about pain assessment in the nonverbal child who has SNI, and as parents are empowered with information. This gap will also continue to close as the number of experts in pediatric pain and palliative care increases.

FINDING THE CAUSE OF PAIN AND OTHER SYMPTOMS

Pain and other distressing symptoms can be treated without identifying a cause. This section highlights how distressing symptoms are both signs of underlying medical problems and indicators of physical discomfort. By taking both into account, we can consider the range of intervention options—those that treat an identified medical problem and those that diminish the associated discomfort and distress.

Children who have SNI are vulnerable to being subjected to exhaustive searches for the medical cause of a problem, such as pain or vomiting, with no consideration or knowledge of symptom management strategies that could be used earlier in the process. Symptom treatment can both improve comfort and indirectly reveal that the cause of the problem has been managed. Pain can trigger some problems, including spasticity, muscle spasms, autonomic dysfunction, and disrupted sleep. Treatment that focuses on an identified problem will not be addressing the cause if pain remains untreated. The goal with all of the distressing symptoms experienced by children who have SNI is to understand what is causing the symptoms so that symptom treatment can be integrated into medical care plans. A few details to highlight these points follow.

Pain

The first step in the process of addressing pain is to search for causes that can be treated, thus eliminating the source of pain. As an example, gastroesophageal reflux disease (GERD) with associated esophagitis is a problem whose first symptom can be pain. Treatment of GERD eliminates pain when GERD is the only cause of pain.

As is reviewed in detail in chapter 4, children who have SNI are also at risk for pain from sources that cannot be identified routinely by medical tests. Examples include central neuropathic pain and visceral hyperalgesia. Being aware of these potential causes of pain allows pain treatment trials to be initiated earlier. Treatment of central neuropathic pain or visceral hyperalgesia does not eliminate the problem, but it does decrease the pain generated by the problem. Starting symptom treatment early in the process of searching for a medical cause of pain will both improve comfort and indirectly indicate the possible source of pain. In addition to providing earlier symptom relief, this approach might also avoid the need for further testing for causes of pain.

Vomiting and retching

Many children who have SNI vomit and retch frequently. As with pain, initial steps in treatment involve evaluation for medical causes of vomiting, including common causes such as constipation and GERD and potentially serious causes such as obstruction of the intestines (bowels). As in managing pain, awareness of symptom treatment options for some causes of vomiting and retching can improve the problems and their accompanying discomfort. Causes include visceral hyperalgesia, autonomic dysfunction, and stimulation of the vomiting reflex. Treatment of these sources is covered in detail in chapters 5 and 7.

Uncomfortable breathing

Uncomfortable breathing is also referred to as dyspnea, respiratory distress, or shortness of breath. This symptom can occur when a child has an acute respiratory illness and when a child has progressive respiratory failure, which can result from SNI. Increased work of breathing, along with other symptoms such as coughing and fever, will prompt the healthcare team to begin treatment for pneumonia.

Children who have SNI may experience shortness of breath as respiratory illnesses become more frequent and severe. There is growing recognition of symptom treatment strategies that can decrease such distress and can be used along with the medical treatment for an acute respiratory illness. Fear of treating uncomfortable breathing with an opioid can prevent the treatment of this significant source of distress for both the child and the family and is an unfortunate barrier to integration of symptom treatment into medical care plans. These fears and strategies for improving comfort are covered in detail in chapter 6.

Spasticity

Many children who have SNI have spasticity. Intermittent muscle spasms are a well-recognized source of discomfort, and pain from other sources can increase the frequency and severity of muscle spasms. As discussed above, it is beneficial to consider all sources of pain, including such causes as central pain. Muscle spasms in some children improve more from medications that treat pain than from medications used for spasticity. This topic is covered in greater detail in chapters 4 and 7.

CONSIDERING BOTH THE MEDICAL CAUSES of each problem and the symptom treatment options will improve the likelihood that the associated distress will be improved. This approach ultimately ensures that two fundamental goals for children who have SNI are integrated: maintaining health when possible and improving comfort throughout life.

WHY CHILDREN WHO HAVE SNI EXPERIENCE SUCH A VARIETY OF DISTRESSING SYMPTOMS

One of the functions of the brain is to process the signals transmitted from the body through the sensory network of nerves. This process involves receptors that receive and send signals and neurotransmitters (chemicals) that inhibit or excite these receptors. As the nerves transmit information, a balance takes place between dampening (inhibition, suppression) and enhancing (excitation, stimulation) these signals. Individuals who have impairment of the brain may have a decrease in the inhibition or an increase in the excitation of such signals. Many of the symptoms seen in children who have SNI reflect an imbalance in the suppression and stimulation of signals to and from the brain. A multitude of features can be produced as a result of these imbalances, both

chronically and intermittently, including central neuropathic pain, muscle spasms, dystonia, and posturing. Understanding that this imbalance can result in symptoms provides the basis for using medications that provide benefit by either enhancing inhibition or decreasing excitation of signals.

In many cases, treatment does not "fix" the cause but rather alters the imbalance, which is one of the challenges of treating these distressing symptoms and problems in children who have SNI. Understanding the benefit and limitations of such interventions can help physicians and empower parents by leading to an understanding of why some children develop symptoms that become intractable to available medical and symptomatic treatments. As described in the discussion of empirical treatment trials later in the chapter, there is a balance between searching for causes and being open to the possibility that the problem is intractable. Recognizing this balance allows physicians and families to consider the diminishing benefit of continued testing and medication trials. When a problem seems intractable, many families are vulnerable to the good intentions of the medical team to "keep looking for answers" or having to accept that there is "nothing more we can do." This critical and challenging topic is covered in greater detail in chapters 5, 7, and 9.

I highlight this information now in order to acknowledge the progressive and persistent nature of problems that can be encountered in children who have SNI. For many of these children, this can be a time of diminishing benefit from the chronic and acute treatment of medical problems, and children then benefit from an increasing emphasis on strategies that improve comfort. Care plans are ideally approached with the goals of (1) minimizing decline in health and maximizing recovery with the use of chronic and acute interventions, (2) being mindful of when the intended benefit is no longer occurring, and (3) utilizing interventions that improve comfort throughout. Figure 1.3 illustrates schematically how, over time, the ability to meet these goals can shift. At such times, parents often simultaneously "hope and prepare."

BARRIERS TO THE USE OF MEDICATIONS FOR PAIN AND OTHER SYMPTOMS

A number of barriers understandably impede the consideration and use of medications for symptom management. Barriers include fear of harm from the medication, fear of drug addiction, and fear of giving up too soon.

Parents and physicians may feel they are "giving up" when they focus on symptom management. Because symptom management is not "fixing" a problem, a view can develop that the child is not being "treated." Even the language used contributes to this view, such as referring to medical "treatment" versus symptom "management." As will become clearer throughout this book, identifying and managing a distressing symptom is as much a form of treating a problem as is evaluating and treating the more commonly recognized medical problems.

There are also many concerns about the risks associated with medications used for symptom treatment. Parents may have seen their child experience excessive sedation or other unwanted effects from medication, making them wary about starting other medication trials. These concerns and fears are best addressed by understanding the medication, including what to expect. For some children, symptom treatment improves the child's level of interaction, once the discomfort is addressed. When sedation does occur, it is typically transient, improving over the first week or with adjustment of the medication dose, if needed. It also helps to recognize that medications used for symptom treatment address the mechanisms that transmit pain and other distressing symptoms, rather than eliminating awareness of the problem through sedation. These mechanisms can involve blocking the receptors that transmit signals or stimulating the receptors that diminish pain perception.

One of the greatest fears surrounding symptom treatment is the risk of respiratory depression (slower or depressed breathing) with the use of opioids. This fear creates an assumption that allowing the benefit of symptom treatment, especially for dyspnea, requires accepting the risk of respiratory depression and, possibly, earlier death. Fortunately, the use of opioids is safer than is often assumed, including for dyspnea. Certainly, safe opioid use requires a knowledge of appropriate dosing and titration (that is, increasing from an initial dose to a dose that provides benefit). Safety measures may include starting at a lower dose and titrating in a standardized manner for individuals with an altered level of alertness or compromised breathing, and adjusting doses for renal (kidney) or hepatic (liver) impairment.

The association of opioid use with end-of-life care can result in an assumption either that opioids hasten death or that someone must be dying when opioids are prescribed. When used appropriately, opioids do not hasten death but can ensure comfort throughout life. The health benefit of symptom treatment has typically not been recognized, but there is a grow-

ing recognition that untreated distress and discomfort can have a negative effect on health (Temel et al. 2010).

In summary, the risk of complications related to medications for symptom management is commonly overstated. Unfortunately and unnecessarily, parents may feel they have to accept excessive risk for the benefit of providing comfort for their child. If a child is experiencing continued discomfort, despite interventions that the medical team is experienced and comfortable with using, it is critical that a physician with greater expertise be brought in to assist with management.

IDENTIFYING A MEDICATION TREATMENT PLAN

Again, the principles discussed in this chapter are intended as a framework for the information provided in later chapters, which includes interventions for maximizing both health and comfort. This section highlights important considerations in symptom evaluation and monitoring.

Empirical treatment trials

Treatment decisions in medicine often involve empirical trials, or what may seem to be a process of trial and error. Though such a trial can give the impression of making random choices, hoping that one intervention will eventually help, it is best viewed as a process based on a knowledge of the possible explanations for a given problem, then a ranking of known interventions according to which is most likely to help and least likely to cause harm.

Many parents are familiar with this process. They get to know the features that indicate a given problem in their child and the interventions that address or help the problem. This process allows parents to identify the interventions they can use at home. One family may learn through trial and error that when their child's arms and legs extend out and become stiff, they can "break" the event by bending the head or legs forward to bring the chin or knees closer to the chest. Another family may learn the positions that are most comfortable for their child. Other strategies can involve adjusting feedings, venting a gastrostomy feeding tube, giving a warm bath, cuddling, swaddling, massage, vibratory stimulation with special mats or pillows, and weighted blankets (Complex Child E-Magazine 2009; Liptak 2005; Lundeberg 1984; Lundeberg et al. 1987).

An empirical approach is often necessary in medicine. It involves weighing the risks and benefits of both the evaluation process and the interventions available to treat potential sources of the problem. In some circumstances, the benefit of a treatment trial is greater than the potential harm of the test used to determine the cause of the problem. At other times, it is not possible to identify with certainty the source of a distressing symptom.

Empirical treatment in medicine can be considered a practical approach to treatment. It is based on using experience and evidence from the medical literature rather than scientific proof of the problem in a particular child. An example to illustrate this process is the treatment of GERD. When a child with SNI has features that suggest GERD, it is common to initiate a medication trial without further tests. This approach reflects the safety of initiating such a trial and the benefit of avoiding diagnostic tests that have potential discomfort or risk, such as endoscopy. Because GERD is a frequent problem in children who have SNI, it is more likely that the symptoms are due to this condition than would be assumed for other groups.

Such an approach is also of great benefit when considering symptom management trials. As an example, when a child with SNI has features that suggest pain, the first step is to consider potential causes of the pain. Tests may be done to look for causes (see table 4.1 and figure 4.2), and treatment for GERD may be started, if the initial test findings are normal.

When the problem persists, a child who has SNI may then undergo multiple and repeated tests. As an alternative, the child may benefit from starting an empirical medication trial—rather than waiting until all possible tests have been obtained—such as a medication for central neuropathic pain. It is certainly important not to miss treatable sources of pain before initiating such a trial. But it can be tremendously helpful to consider an empirical pain treatment trial after serious causes have been tested for, and to start the trial while considering other tests. Just as with GERD, improvement provides indirect evidence that the intervention has addressed the problem. Chapter 4 covers this process in greater detail, with suggestions for each of the steps in the process.

Ideally, an empirical treatment plan is a process based on full knowledge of medical causes and symptom strategies, including the risks and benefits of tests and interventions. Throughout the process, the following questions can help everyone involved consider the options:

- What are possible explanations for the problem / distressing symptom that has been identified?

- What can be learned from a test, such as blood work or other studies?
- What will not be learned from this test?
- What discomfort or harm can be caused by the test?
- What will be done with the information obtained from the test?
- Will the treatment plan be altered by the test results?
- Are there empirical treatment trials to consider before pursuing further testing?
- At what point are the tests and treatments being done just for the sake of "doing something"?

The information provided in later chapters is intended to help with the process of weighing the risks and benefits of the various treatments and tests that are used for children who have SNI.

Medication options for symptom management

Table 3.4 provides a summary of medications for symptom treatment, including the mechanism of action of the medication and other details. This is information that can be shared and discussed with a child's medical team. As discussed in chapter 1, parents are empowered when they have access to information. Yet this empowerment must be balanced with a parent's not feeling responsible for monitoring all details of his or her child's healthcare.

Medications for symptom treatment in children who have SNI include gabapentin, nortriptyline, tramadol, morphine, benzodiazepines, clonidine, cyproheptadine, and anticholinergics. Other medications require greater expertise in use (methadone), or their use is not as well established in children (tizanidine, dronabinol and SNRIs). Experts in the use of all these medications, such as palliative care physicians, can assist a child's medical team with selection and use. (These medications are covered in greater detail in subsequent chapters.)

Drug metabolism and interactions with other drugs are discussed below, followed by a summary of the steps involved in assessing the benefit of a medication and the process of discontinuing a medication that is not providing the intended benefit. This last point is essential, as it is far too common to see a medication continued even when it is unclear whether the drug is providing any benefit—a situation in which the risk of the medication outweighs the intended benefit.

TABLE 3.4 Medications to consider for symptom management

Medications	Evidence for use	Comments
Gabapentinoids: Thought to inhibit excitation by binding to the alpha-2-delta subunit of voltage-dependent Ca^{2+} ion channels in the CNS		
Gabapentin (Neurontin) Pregabalin (Lyrica)	Neuropathic pain Central pain Visceral hyperalgesia Dysautonomia Spasticity	• Side effects include sedation, nystagmus (jerky eye movements), tremor, swelling • Sedation can be minimized by increasing the dose gradually and then advancing more rapidly as tolerated • Both now available as a liquid • No significant interactions with other drugs • No evidence that one is superior to the other for children who have SNI
Tricyclic antidepressants (TCAs): Reuptake inhibition of serotonin and norepinephrine in the CNS, both inhibitors of pain transmission (also antagonists of 5HT-2, H-1, and Ach)		
Nortriptyline (Pamelor) Amitriptyline (Elavil)	Neuropathic pain Central pain Visceral hyperalgesia	• Side effects include dry mouth, constipation, urinary retention, sedation, agitation, akathisia (restlessness) • Limit the use of other anticholinergic medications • Side effects can be lessened by increasing gradually • Caution when using with other medications that increase serotonin levels, creating risk of serotonin syndrome • Risk of prolonged QT syndrome, most likely when used with other drugs with same risk

TABLE 3.4 *(continued)*

Medications	Evidence for use	Comments
		• Serum level not necessary, though can document absorption and minimize toxicity
Serotonin-norepinephrine reuptake inhibitors (SNRIs): Reuptake inhibition of serotonin and norepinephrine		
Venlafaxine (Effexor) Duloxetine (Cymbalta)	Neuropathic pain in adults (first- or second-line therapy)	• Limited information on use in children • Not available as liquid • Cymbalta is an extended-release capsule that cannot be crushed • Caution when using with other medications that increase serotonin levels, creating risk of serotonin syndrome • Side effects similar to TCAs
Opioids: Opioid receptor agonists, including mu receptors		
Tramadol (Ultram)	Pain	• Tramadol may have added benefit, given its multiple properties (mu opioid receptor agonist, serotonin-releasing agent, norepinephrine reuptake inhibitor) • Caution with tramadol includes its use for patients with seizures and use with other drugs that cause serotonin syndrome • Morphine and other opioids safe when started with a standard dose, titrated to effect, and adjusted for renal impairment and respiratory depression, for example
Morphine	Pain Dyspnea Autonomic storms	
Methadone	Pain Neuropathic pain	

(continued)

TABLE 3.4 *(continued)*

Medications	Evidence for use	Comments
		• Methadone may have benefit for neuropathic pain as an NMDA receptor antagonist; requires expertise in use
Benzodiazepines: Increase affinity of GABA for $GABA_A$ receptors		
Clonazepam (Klonopin)	Myoclonus Potential pain adjuvant	• All can result in tolerance with chronic use • All can result in paradoxical effects, such as increased agitation and irritability • Midazolam, diazepam, and clonazepam metabolism is altered by P450 enzyme inducers and inhibitors • Lorazepam metabolism is not altered • Clonazepam has a risk of increased respiratory secretions • Midazolam is very lipid-soluble, resulting in rapid onset as well as accumulation with daily use
Diazepam (Valium)	Spasticity	
Lorazepam (Ativan)	Dyspnea	
Midazolam (Versed)	Agitation	
All	All can be considered for intermittent autonomic storms and intermittent muscle spasms	
Alpha-2 adrenergic receptor agonists		
Clonidine (Catapres)	Dysautonomia Spasticity May enhance pain management	• Side effects include hypotension (low blood pressure), bradycardia (low heart rate), sedation, irritability, though fewer side effects in children than in adults • Side effects can be minimized by increasing the dose gradually • Tizanidine not well studied in children
Tizanidine (Zanaflex)	Spasticity May enhance pain management	

TABLE 3.4 *(continued)*

Medications	Evidence for use	Comments
		• Tizanidine has a risk of elevated liver transaminases (measured in the blood), though mostly in combination with other medications that have a risk of liver toxicity • Clonidine has the advantage of delivery options (liquid and transdermal patch)
Antiemetics: Serotonin-2 and -3, histamine-1, muscarinic (acetylcholine), and dopamine-2 receptor antagonists (blockers)		
Cyproheptadine (Periactin) Ondansetron (Zofran) Metoclopramide (Reglan)	Dysautonomia Retching in children who have SNI Vomiting Delayed motility Vomiting	• Cyproheptadine (5HT-2, H-1, and Ach) may be beneficial when associated features with dysautonomia include hypothermia or retching • Ondansetron (5HT-3) can result in constipation • Metoclopramide (D-2) can result in irritability and dystonic reactions, occurring at a higher rate in children and with prolonged use
Anticholinergics: Acetylcholine receptor blockers		
Glycopyrrolate (Robinul) Hyoscyamine (Levsin) Atropine Scopolamine	Secretion management Antispasmodics	• Side effects include constipation, urinary retention, paradoxical agitation • Care must be taken to minimize secretions that become thick and difficult to mobilize • Unclear benefit as antispasmodics of the gut

(continued)

TABLE 3.4 *(continued)*

Medications	Evidence for use	Comments
		• Hyoscyamine and atropine can be given sublingually; scopolamine available as a transdermal skin patch
Cannabinoids: Cannabinoid receptor agonist (C-1 and C-2)		
Dronabinol (Marinol)	Central pain in adults with multiple sclerosis Appetite stimulant	• Limited studies in children • Side effects include delayed gastric emptying, dizziness, anxiety, depression, irritability, restlessness, tachycardia, dry mouth

Note: For those seeking more specific information about medications, you will find tables with medications and dosages at www.press.jhu.edu/CaringforChildrenWhoHaveSevere NeurologicalImpairment.
Abbreviations: 5HT, serotonin; Ach, acetylcholine; C, cannabinoid; D, dopamine; H, histamine; NMDA, *N*-methyl-D-aspartate.

Drug interactions and metabolism

When prescribing medications, it is useful to first consider the different mechanisms of action, to avoid using several medications with the same properties. As an example, TCAs have many properties, including anticholinergic, in addition to those that make them beneficial for central neuropathic pain and visceral hyperalgesia. The associated side effects of dry mouth, slower intestinal motility, constipation, urinary retention, increased body temperature, and agitation will be increased if a patient is already taking an anticholinergic medication or starts taking one later.

Use of these and other medications also requires consideration by physicians and pharmacists of how drugs are eliminated from the body, a process referred to as drug metabolism and clearance (Lynch and Price 2007; Wilkinson 2005). Drug metabolism and clearance occur in a variety of ways. Individual genetic variations can influence drug metabolism and therefore influence how an individual responds to a particular drug. Genetic variations should be considered when an individual is noted to have an

unusual sensitivity or resistance to drug effects at a standard dose. As an example, 7% of Caucasians are poor metabolizers of drugs dependent on CYP2D6, an enzyme in the liver that metabolizes many antidepressants and opioids.

Medications can inhibit or induce these drug-metabolizing enzymatic systems, altering the effect of other drugs that are metabolized through the same systems. Inhibitors generally lead to an increased drug effect through a decrease in metabolism, unless the drug is inactive until it is metabolized to its active form. Inducers generally lead to a decreased drug effect through an increase in metabolism, again, unless the drug starts out as inactive until metabolized. Here are some examples of these effects:

- Codeine: This is a prodrug (a drug that is inactive until metabolized to its active form) that is ineffective in up to one-third of individuals, as a result of their inability to metabolize codeine to the active metabolite, morphine. Codeine can result in toxicity in individuals who are ultrarapid metabolizers (Ciszkowski et al. 2009; Williams, Patel, and Howard 2002).
- Carbamazepine: Erythromycin is an enzyme inhibitor that can cause carbamazepine toxicity.
- Midazolam, diazepam, or clonazepam: Sedation can increase with some enzyme inhibitors, including erythromycin and antifungals (fluconazole, ketoconazole), and withdrawal symptoms are possible with some enzyme inducers, including phenobarbital, phenytoin, and carbamazepine (Riss et al. 2008).

Detailed information about P450 (an enzyme system involved in drug metabolism in the liver) and drug interactions is available for physicians through Indiana University (2011). For children who have SNI, the most common drugs to consider in this category include the following:

- Enzyme inhibitors: ciprofloxacin, erythromycin, fluconazole, ketoconazole, valproic acid, SSRIs, omeprazole, metronidazole
- Enzyme inducers: phenobarbital, phenytoin, carbamazepine, oxcarbazepine
- Medications that can be altered by enzyme inhibitors and inducers (referred to as substrates): TCAs (amitriptyline, nortriptyline), tramadol, benzodiazepines (excluding lorazepam), risperidone, carbamazepine, phenytoin

Prolonged QT interval

Some medications have an identified risk of prolonging the QT interval, as measured on an ECG. A prolonged QT interval can place a person at risk for an abnormal rhythm of the heart and, rarely, sudden death. This risk can be minimized by identifying children at risk and avoiding medication combinations that increase the risk. A useful summary of medications to consider can be found at www.qtdrugs.org. Drugs posing this risk that are more likely to be used in children who have SNI include erythromycin, methadone, risperidone, ciprofloxacin, levofloxacin, ketoconazole, TCAs, and SSRIs. Some drugs have a low risk, with significant risk occurring only when one such drug is used along with another drug also carrying the risk of prolonged QT interval. For medications with a greater risk, an ECG can determine whether a child has a preexisting prolonged QT interval. In most children, the QT interval is normal and these medications can be used safely. As with other drug interactions, risk is decreased by avoiding the simultaneous use of two drugs with the same risk, by knowing the safe dose range, and by avoiding starting or stopping other medications that alter a drug's metabolism.

Summary of medication interactions

Information on drug interactions can be both overwhelming and paralyzing, and it is imperative that parents should not feel responsible for knowing these details. The goal of including such information here is simply to enhance a general understanding of the safe utilization of medications with potential benefit for children who have SNI. Without this information, a physician or parent might avoid a medication with potential benefit, out of fear about the potential harm. Alternatively, the risk associated with a medication can be increased by not considering these interactions, increasing the chance that a medication with potential benefit will not be continued or will cause preventable harm to a child.

Scheduled daily medication versus as-needed medication

In symptom treatment, some children benefit from a scheduled medication, to minimize the symptom or keep it from occurring. Some symptoms can be treated "in the moment" with a medication used when needed, referred to as prn (*pro re nata*, "as the circumstance arises"). In general, the

decision is based on weighing the benefit of using an intervention to minimize symptom occurrence versus the risk of the scheduled medication. Several types of information can be used as a guide:

- Frequency of the symptoms: the more frequent the symptom, the greater the benefit from a scheduled medication
- Severity and duration of the symptoms: the greater the severity and duration of each episode, the greater the benefit from a scheduled medication
- Response to the prn medication: as an example, autonomic "storms" that occur once or twice a week and respond well to as-needed clonidine, with symptoms consistently resolving within 30 minutes of giving the prn clonidine dose

Monitoring for the outcome from a medication

One of the most important steps in avoiding an excessive number of medications is to establish a rigorous process before starting a medication. This process should be considered to be as important as determining the medication option for the problem identified. A defined process can improve the ability to assess whether the outcome with the medication recommends its continued use.

The first step involves defining the problem being treated and the baseline features of that problem. The most rigorous approach is the use of a validated scale to measure the severity of the symptom. The only such scales available for children who have SNI are the pain assessment tools described earlier in this chapter. Even when a scale is not available, however, some routine questions can define the overall severity of the problem, along with the frequency and duration of a typical episode. This baseline information can then be used to "measure" and follow the degree of benefit from any treatment.

The next step is to define the minimum dose for the medication trial and the time frame in which benefit is expected to occur. Factors that determine the minimum length of a trial include the need to titrate the medication dose over time, to avoid problems such as sedation; the average time to onset of benefit; and the frequency of symptoms. As an example, some children have problems that occur in a cycle, such as intermittent pain episodes over 5 to 7 days, occurring every 3 to 4 weeks. In this example, a longer trial of 3 to 4 months will be needed for the child to experience a sufficient number of potential pain episodes while the

medication's utility in decreasing the frequency, duration, and severity of these events is monitored. In contrast, a shorter trial is needed for a child who experiences daily pain episodes. The goals are (1) to avoid an inadequate trial, as can occur if the duration of the trial is too short or the dose of the medication is insufficient for the problem, and (2) to avoid continued use of a medication with inadequate benefit for treating the problem.

Documentation of this information is beneficial. Physicians, social workers, and care coordinators can facilitate the creation of a table that provides a summary of information. Useful information includes the start date, reason for use, and a summary of the benefit identified, as well as the stop date and the reason the medication was discontinued. Though this process takes extra effort up front, it can minimize potentially harmful decisions in the future. Such a table is particularly helpful for children who have SNI, given the large number of healthcare providers often involved in a child's care. It can help avoid stopping a medication that has shown benefit or starting a medication with a mechanism of action similar to that of a previous medication that gave no benefit.

Steps to starting and stopping medications for symptom management

1. Determine the presence of a symptom causing distress.
2. Describe the severity of the symptom, and the frequency and duration of episodes.
3. Evaluate for potential causes of the symptom.
4. Treat identified causes when possible and if consistent with the goals of care.
5. Utilize available symptom treatment interventions.
6. Review current and previous medications, to avoid using medications with the same mechanism of action (indicated in medication tables).
    a. The simultaneous use of two medications with the same mechanism of action increases the risk of side effects from that mechanism of action.
    b. Avoid multiple trials of medications with the same mechanism of action; consider a trial of medication with the same mechanism of action as a prior medication if the new medication also has other properties not yet tried.

7. Review current medications for possible drug-drug interactions, such as the use of a medication that can alter the metabolism of other medications.
8. Review any prior experience with sedating medications to guide initial dosage.
9. Identify the timeframe in which an intervention is expected to provide improvement.
    a. Depends on the onset of benefit and the need to titrate a medication:
        i. Hours to days: opioid, benzodiazepine, sucralfate
        ii. 3 to 7 days: proton pump inhibitor (PPI), cyproheptadine
        iii. 1 to 3 weeks: gabapentin, TCA, SNRI
    b. Depends on the frequency of symptoms: shorter trial if symptoms occur daily; longer trial if symptoms are cyclical, such as several days every other week
10. Assess for improvement.
    a. Have the features indicating the symptom or problem improved? Examples:
        i. Crying, grimacing, spasms, and arching associated with pain
        ii. Retching, flushing, sweating, and stiffening with autonomic dysfunction
        iii. Agitation and distressed look with dyspnea
    b. How much improvement in severity or decrease in frequency and duration of symptoms would you estimate: Is your child 25% improved, 50% improved, greater than 50% improved, mostly resolved?
11. Conduct follow-up.
    a. Monitor for side effects that may prohibit continued use of a medication.
    b. If there is some but not full benefit, assess whether the medication will be continued or discontinued before initiating a new medication trial.
        i. Adding a medication with a different mechanism of action may be beneficial when there was partial benefit from the initial drug. As an example, one study identified that gabapentin with nortriptyline provided greater benefit for neuropathic pain in adults than did either medication alone (Gilron et al. 2009).

c. The length of time to continue a medication that is providing benefit is unclear.
    i. In children still growing, continuing the same dose without adjusting it for weight gain can indicate continued benefit if symptoms return as the child "outgrows" the dose.
    ii. In general, 12 months of improved symptom control can be a reasonable duration for children with static CNS conditions and stable health before considering discontinuing or tapering a medication, being prepared to increase or restart if symptoms return. The severity and length of symptoms should also be considered.
    iii. Children who have diseases or clinical features with neurodegeneration or who have declining health are likely to benefit from continuation of the medication(s).
d. If an intervention is discontinued, assess whether the drug requires tapering before stopping (drugs to taper when used for 1 to 2 weeks or longer include baclofen, benzodiazepines, opioids, gabapentin, clonidine, TCA, SNRI, SSRI).

Tapering medications safely before stopping

If they are discontinued suddenly or tapered too quickly, some medications can cause a discontinuation syndrome or rebound of symptoms. The withdrawal symptoms can adversely affect health and can be a source of distress and discomfort (table 3.5). Discontinuation syndrome or rebound of symptoms can create a false assumption that the medication was treating the problem and therefore was providing benefit.

The risk of withdrawal symptoms and the duration of tapering depend on the specific medication and how long the child has been taking it. In general, baclofen, clonidine, and gabapentin can be tapered off over 2 to 4 weeks, such as decreasing by 10% to 20% of the initial dose every 2 to 4 days, whereas benzodiazepines, opioids, and TCAs usually require longer tapering, often over 6 to 12 weeks (Ducharme et al. 2005; Fisher 2010; Lader, Tylee, and Donoghue 2009; Leo and Baer 2005; Shelton 2001). The few studies available provide the following information:

- Guidelines identified for patients in the intensive care unit (ICU) who have received a continuous infusion of an opioid or benzodiazepine: For 1 to 3 days duration, decrease by 20% of the original dose

TABLE 3.5 Medication withdrawal symptoms

Drug category	Features
Baclofen	Agitation, confusion, hallucinations, insomnia, hyperthermia, seizures, rebound spasticity, muscle rigidity
Clonidine	Rebound hypertension (increased blood pressure)
TCAs	Agitation, irritability, disrupted sleep, GI distress, tremor, sweating
Opioids	Agitation, restlessness, grimacing, inconsolable crying, disrupted sleep, muscle spasms, seizures, increased heart rate and blood pressure, increased respiratory rate, vomiting, gagging, diarrhea, cramps, hiccups, goose bumps, shivering, fever, tears, runny nose, yawning, sweating, dilated pupils
Benzodiazepines	Jitteriness, agitation, increased heart rate, muscle cramps, disrupted sleep, heightened sensitivity to light and sound

each day; 4 to 7 days, decrease by 13% to 20% of the original dose each day; 8 to 14 days, 8% to 13%; 15 to 21 days, 3% to 8%; more than 21 days, 3% (Ducharme et al. 2005).

- Patients receiving a long-term oral benzodiazepine benefit from a taper over 8 to 12 weeks, done as a decrease every 7 days by an amount that is 10% of the initial dose; for some patients, a longer taper, up to 6 months in duration, may be needed, such as a decrease by 5% of the initial dose every 7 days (Lader, Tylee, and Donoghue 2009).
- TCA doses can be lowered every 5 to 7 days over a minimum of 2 weeks, though some patients will require a slower taper over 1 to 3 months (Shelton 2001).
- *Most important:* (1) Monitor for withdrawal symptoms and adjust the wean schedule as needed, and (2) consider other sources of the symptoms identified.

TAKE-HOME POINTS

- When exploring interventions for acute and chronic problems, consider treatment options for both medical problems and distressing symptoms.

- Physicians and other professionals caring for children who have SNI must become familiar with the behaviors that suggest pain when a child is unable to communicate about pain.
- Parents can be empowered with knowledge about pain behaviors by sharing information in pain assessment tools, such as the R-FLACC and INRS.
- Information in chapter 4 reviews the steps to take when concerns about pain are identified.
- Physicians and other professionals caring for children who have SNI should become experienced with symptom management or should use experts, such as palliative medicine clinicians, to avoid a delay in benefit due to fear of harm.
- Focusing on a finite number of medications can improve safety and the ability to improve comfort; medications most commonly reviewed in subsequent chapters include gabapentin, nortriptyline, tramadol, morphine, benzodiazepines, clonidine, and cyproheptadine.
- Approach empirical (trial-and-error) treatment in a systematic way by considering the risks and benefits of the options available.
- Consider the mechanism of action of each intervention, both to minimize medication toxicity and to avoid a delay in potentially beneficial treatment with an intervention having a different mechanism of action.
- Define the criteria for continuing and discontinuing a medication when starting a medication, to minimize the harm from unnecessary polypharmacy.
- Some medications require careful tapering before discontinuing.
- Nonpharmacological interventions are always an important part of symptom management.
- Many of the distressing symptoms in children who have SNI are a result of the impaired central nervous system; medications are available to improve comfort, but they will not "fix" or remove the source of the problem.
- Repeated testing when symptoms persist despite evaluation and treatment can result in greater harm than benefit.
- Use expertise, such as pediatric palliative care, for symptoms that are difficult to control.
- When there is declining benefit from the array of interventions, what is hoped for can shift from maintaining health and comfort to a primary goal of comfort.

References

Breau LM, Finley GA, McGrath PJ, Camfield CS. 2002 Validation of the Non-communicating Children's Pain Checklist-Postoperative Version. *Anesthesiology* 96(3):528–35.

Breau LM, McGrath PJ, Camfield C, et al. 2000. Preliminary validation of an observational pain checklist for persons with cognitive impairments and inability to communicate verbally. *Dev Med Child Neurol* 42(9):609–16.

Breau LM, McGrath PJ, Camfield CS, Finley GA. 2002. Psychometric properties of the Non-communicating Children's Pain Checklist-Revised. *Pain* 99(1-2):349–57.

Carter B, McArthur E, Cunliffe M. 2002. Dealing with uncertainty: parental assessment of pain in their children with profound special needs. *J Adv Nurs* 38(5):449–57.

Ciszkowski C, Madadi P, Phillips MS, et al. 2009. Codeine, ultrarapid-metabolism genotype, and postoperative death. *N Engl J Med* 361(8):827–28.

Complex Child E-Magazine. 2009. Vibration for pain control and calming. www.articles.complexchild.com/sept2009/00152.html.

Ducharme C, Carnevale FA, Clermont MS, Shea S. 2005. A prospective study of adverse reactions to the weaning of opioids and benzodiazepines among critically ill children. *Intensive Crit Care Nurs* 21(3):179–86.

Fisher D. 2010. Opioid tapering in children: a review of the literature. *AACN Adv Crit Care* 21(2):139–45.

Gilron I, Bailey JM, Tu D, et al. 2009. Nortriptyline and gabapentin, alone and in combination for neuropathic pain: a double-blind, randomised controlled crossover trial. *Lancet* 374(9697):1252–61.

Hadden KL, von Baeyer CL. 2002. Pain in children with cerebral palsy: common triggers and expressive behaviors. *Pain* 99(1–2):281–88.

Hunt A, Goldman A, Seers K, et al. 2004. Clinical validation of the paediatric pain profile. *Dev Med Child Neurol* 46(1):9–18.

Hunt A, Wisbeach A, Seers K, et al. 2007. Development of the paediatric pain profile: role of video analysis and saliva cortisol in validating a tool to assess pain in children with severe neurological disability. *J Pain Symptom Manage* 33(3):276–89.

Indiana University, Department of Medicine, Division of Clinical pharmacology. 2011. P450 drug interaction table. http://medicine.iupui.edu/clinpharm/ddis/table.aspx.

Lader M, Tylee A, Donoghue J. 2009. Withdrawing benzodiazepines in primary care. *CNS Drugs* 23(1):19–34.

Leo RJ, Baer D. 2005. Delirium associated with baclofen withdrawal: a review of common presentations and management strategies. *Psychosomatics* 46(6):503–7.

Liptak GS. 2005. Complementary and alternative therapies for cerebral palsy. *Ment Retard Dev Disabil Res Rev* 11(2):156–63.

Lundeberg T. 1984. Long-term results of vibratory stimulation as a pain relieving measure for chronic pain. *Pain* 20(1):13–23.

Lundeberg T, Abrahamsson P, Bondesson L, Haker E. 1987. Vibratory stimulation compared to placebo in alleviation of pain. *Scand J Rehabil Med* 19(4):153–58.

Lynch T, Price A. 2007. The effect of cytochrome P450 metabolism on drug response, interactions, and adverse effects. *Am Fam Physician* 76(3):391–96.

Malviya S, Voepel-Lewis T, Burke C, et al. 2006. The revised FLACC observational pain tool: improved reliability and validity for pain assessment in children with cognitive impairment. *Paediatr Anaesth* 16(3):258–65.

Oberlander TF, Gilbert CA, Chambers CT, et al. 1999. Biobehavioral responses to acute pain in adolescents with a significant neurologic impairment. *Clin J Pain* 15(3): 201–9.

Riss J, Cloyd J, Gates J, Collins S. 2008. Benzodiazepines in epilepsy: pharmacology and pharmacokinetics. *Acta Neurol Scand* 118(2):69–86.

Shelton RC. 2001. Steps following attainment of remission: discontinuation of antidepressant therapy. *Prim Care Companion J Clin Psychiatry* 3(4):168–74.

Solodiuk JC, Scott-Sutherland J, Meyers M, et al. 2010. Validation of the Individualized Numeric Rating Scale (INRS): a pain assessment tool for nonverbal children with intellectual disability. *Pain* 150(2):231–36.

Stallard P, Williams L, Velleman R, et al. 2002. Brief report: behaviors identified by caregivers to detect pain in noncommunicating children. *J Pediatr Psychol* 27(2):209–14.

Svedberg LE, Englund E, Malker H, Stener-Victorin E. 2008. Parental perception of cold extremities and other accompanying symptoms in children with cerebral palsy. *Eur J Paediatr Neurol* 12(2):89–96.

Temel JS, Greer JA, Muzikansky A, et al. 2010. Early palliative care for patients with metastatic non-small-cell lung cancer. *N Engl J Med* 363(8):733–42.

Wilkinson GR. 2005. Drug metabolism and variability among patients in drug response. *N Engl J Med* 352(21):2211–21.

Williams DG, Patel A, Howard RF. 2002. Pharmacogenetics of codeine metabolism in an urban population of children and its implications for analgesic reliability. *Br J Anaesth* 89(6):839–45.

Pain
Evaluation and Treatment

Although the world is full of suffering, it is also full of the overcoming of it.
—Helen Keller

Physical comfort is a fundamental goal in caring for children who have severe neurological impairment. Unfortunately, parents of these children too often find it challenging to maintain this goal. Despite the significance of pain in children who have SNI, they remain vulnerable to a lack of recognition and treatment of their pain, with parents saying their children have "learned to live with pain" (Carter, McArthur, and Cunliffe 2002).

This chapter begins with a comprehensive review of the sources of pain to consider in children who have SNI, including commonly recognized sources such as gastroesophageal reflux disease (GERD), spasticity, and hip subluxation. Much of the information then focuses on children with pain behaviors that continue despite a search for and treatment of identified sources; various terms are used to describe the behaviors of such children, including "screaming of unknown origin" (Greco and Berde 2005) and neuro-irritability. The chapter provides a framework for treating pain and discomfort in children with SNI.

Several case examples illustrate the challenge of meeting the goal of improving comfort in such children and adults.

Lars, a 3-year-old boy who has SNI as a result of cytomegalovirus (CMV) infection during pregnancy, is admitted to the hospital several times with prolonged episodes of crying, pain that is localized to his abdomen, and difficulty tolerating his tube feedings. Evaluation includes multiple blood tests, abdominal X-rays, pH probe, endoscopy, impedance study, Meckel scan, renal ultrasound, lumbar puncture, and magnetic resonance imaging (MRI). All study findings are unremarkable, except for changes on the head MRI that are consistent with in utero CMV infection. The boy's symptoms persist despite

treatment for constipation, GERD, and spasticity, and the use of morphine sulfate.

Raymond is a 15-month-old who has trisomy 18. He develops increasing, nonspecific irritability and impaired sleep. He has no improvement with treatment of constipation, GERD, and spasticity.

Dylan is a 9-month-old boy who has hypoxic ischemic encephalopathy (HIE). He is receiving treatment for spasticity and GERD. He is hospitalized because of increasing episodes of arching and stiffening over the past two months, thought to be secondary to his GERD. Findings on EEG (electroencephalogram) are negative for seizures. His proton pump inhibitor dose is increased and metoclopramide is initiated, medications that decrease stomach acid and increase emptying of the stomach into the intestines. His diazepam dose is increased to treat the increased stiffening. Despite placement of a jejunostomy tube (J tube) and an empirical trial of metronidazole for small bowel bacterial overgrowth, Dylan continues to have arching, stiffening, and vomiting. He is being considered for Nissen fundoplication surgery.

Grace is a 2-year-old who has leukoencephalopathy of unknown etiology, with associated hypotonia and intellectual disability. She develops persistent irritability and disrupted sleep, with discomfort that is associated with tube feedings, intestinal gas, and bowel movements. There is no identified source of pain and no improvement with empirical interventions, including treatment for GERD and constipation.

Ellen is a 26-year-old who has cerebral palsy and intellectual impairment. Over the past six months, her caregivers have become concerned that Ellen is depressed, as she is withdrawn and not "herself." An evaluation reveals no explanation for these changes. She is first treated with scheduled ibuprofen and later with an antidepressant (a selective serotonin reuptake inhibitor), with minimal benefit noted.

CHILDREN WHO HAVE SNI HAVE A HIGHER RATE AND INTENSITY OF PAIN

In a large population-based survey, 12% of all children experienced pain weekly (Perquin et al. 2000). In marked contrast, pain was found to occur weekly in 44% of children with moderate to profound cognitive impairment and almost daily in 41% to 42% of children with greater impairment

(Breau et al. 2003; Hunt et al. 2004; Stallard et al. 2002). In another study, over a four-week period, pain was noted to occur "once or twice" to "a few times" in 44% and "fairly often" to "every / almost every day" in 21% of children with moderate to severe cerebral palsy (Houlihan et al. 2004).

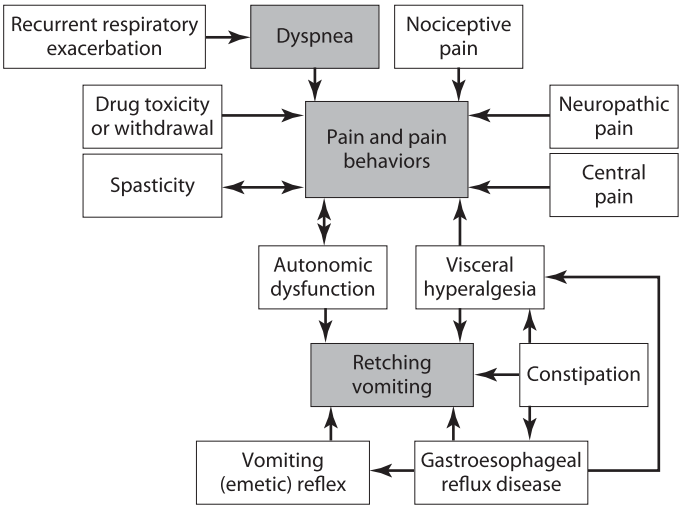
Pain frequency and severity are found to be higher in children with the greatest neurological impairment (Breau et al. 2001; Breau et al. 2003; Houlihan et al. 2004; Hunt et al. 2007; Svedberg et al. 2008). As an example, pain was noted in 48% of ambulatory children with cerebral palsy, compared with a rate of 79% in a nonambulatory group (Svedberg et al. 2008).

In addition to pain being a frequent problem, pain intensity in children who have SNI is rated as high. In a study of children with severe cognitive impairment, the average pain intensity for all sources of non-accidental pain was 6.1 (0 to 10 pain scale; 0 = no pain, 10 = worst pain), with an average duration of 6 hours (Breau et al. 2003). In those with less impairment—specifically, an ambulatory group with accidental pain—the average pain intensity was 3.8, with an average duration of 46 minutes. The highest pain rating in this study, with a mean intensity of 8.7, was in those without an identified source of pain.

This summary of information provides an important reminder that pain is a significant problem for children who have SNI. In the following sections, I review the sources of pain that should be considered and provide guidelines for stepwise management.

SOURCES OF PAIN IN CHILDREN WHO HAVE SNI

Pain is defined by the International Association for the Study of Pain (IASP) as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage. The inability to communicate verbally does not negate the possibility that an individual is experiencing pain and is in need of appropriate pain-relieving treatment" (IASP 2011). Pain can be divided into two types, depending on how the pain is generated in the body: *nociceptive pain* and *neuropathic pain*. Nociceptive pain is a normal and expected pain response to injury or inflammation of tissue in the body. It warns of tissue damage through specialized nerve endings that send pain messages from the site of injury to the central nervous system. Neuropathic pain, on the other hand, arises from changes in the nervous system that result in abnormal transmission of pain signals. This type of pain does not involve ongoing tissue injury. Neuropathic pain can include an increased response to a



Source	Comments	Treatment
Nociceptive pain	Tissue injury and inflammation (table 4.1)	Treat cause; analgesics—medications for pain (figure 4.3)
Drug toxicity or withdrawal	Features of both include behaviors associated with pain	Discontinue drug or alter taper schedule (table 4.2 and 4.3)
Neuropathic pain	Can develop following surgery	Gabapentin, TCA
Central pain, visceral hyperalgesia	Both can result in painful symptoms triggered by normal distension of the GI tract	Gabapentin, TCA
Retching, vomiting	Common in children with SNI, often with associated discomfort (see table 5.1)	Treat possible sources: GERD, visceral hyperalgesia, dysautonomia, receptors involved in stimulation of vomiting center
Autonomic dysfunction (dysautonomia)	Associated features: sweating, flushing (red skin), retching, increased heart rate, agitation, arching, stiffening	*Scheduled:* gabapentin, clonidine, cyproheptadine *Intermittent:* clonidine, morphine sulfate, diazepam
Spasticity	Other pain sources can increase frequency and severity of muscle spasms	Tizanidine, clonidine, gabapentin, short-term and intermittent diazepam, empirical treatment of pain sources such as central neuropathic pain
Dyspnea	Pain sources identified by parents included "chest infection" and "respiratory"—probably reflecting dyspnea (Breau et al. 2003; Hunt et al. 2004)	Fan, as-needed morphine sulfate, as-needed benzodiazepine such as midazolam or lorazepam (see chapter 6)

Figure 4.1. Sources of pain and pain behaviors

painful stimulus, referred to as *hyperalgesia*, or pain due to a stimulus that does not normally provoke pain, referred to as *allodynia*.

I review here the causes of pain, both nociceptive and neuropathic, to consider when caring for children who have SNI, then in the next section provide a guide to pain treatment. Other problems that can result in pain behaviors (figure 4.1) are also covered in this and in subsequent chapters.

One challenge when considering causes of pain and discomfort in nonverbal children who have SNI is distinguishing between when a problem is the cause of pain and when a problem is worsened by pain. As an example, muscle spasms can result in discomfort, and pain from other causes can result in an increase in the frequency and severity of muscle spasms. Similar problems include autonomic dysfunction and dystonia; they can be sources of discomfort, increase as a result of pain from a different source, and have features that are similar to behaviors associated with pain. Comfort can be improved for each child by considering, simultaneously, interventions for each problem and medications that treat pain.

Nociceptive pain: causes of tissue injury and inflammation

New acute pain can be a result of common childhood problems such as an ear infection. Children who have SNI are also at increased risk for such problems as bone fracture, urinary tract infection (UTI), acute pancreatitis, and nephrolithiasis. Problems that may be recurrent and chronic sources of pain include hip subluxation, muscle spasms, GERD, and constipation. Some problems, such as hip subluxation, can be an incidental finding and not the source of pain. Information to suggest this is the pain source would be pain associated predominantly with movement of the hip, such as during transfers, diapering, and clothing changes. Table 4.1 summarizes the pain sources to consider. (See figure 4.2 for a guide to the evaluation process, including guidelines for initial tests.)

Neuropathic pain (peripheral and central)

Neuropathic pain, also referred to as neurogenic pain, is a result of damage to or dysfunction of the peripheral nerves (*peripheral neuropathic pain*) or the CNS (*central neuropathic pain*). This is an important pain source to consider for children with SNI who have unexplained persistent pain behaviors. As described earlier, neuropathic pain can result in an increased response to a painful stimulus (hyperalgesia). Hyperalgesia is suggested by the significant intensity and duration of symptoms in

TABLE 4.1 Sources of nociceptive pain (tissue injury and inflammation)

Source	Reason for considering
Dental	Routine dental care more challenging
Gastroesophageal reflux disease (GERD)	Common in children who have SNI; visceral hyperalgesia can increase the severity of symptoms from GERD
Constipation	Common in children who have SNI; visceral hyperalgesia and central neuropathic pain can increase symptoms that are generated from distension of the colon
Gallstones	Experience suggests more common in tube-fed children; associated with some diseases, including Rett syndrome and metachromatic leukodystrophy (MLD)
Pancreatitis	Associated with valproic acid and prolonged hypothermia (low body temperature)
Bladder distension	More common in children who have SNI; central neuropathic pain can increase symptoms from bladder distension
Bladder infection (UTI)	Increased risk associated with retention of urine
Kidney stones (nephrolithiasis)	Associated with the ketogenic diet, recurrent UTI, and topiramate
Fracture	Increased risk in non-weight-bearing children who have SNI; increased risk of osteoporosis associated with phenobarbitol, phenytoin, carbamazepine, valproic acid
Hip subluxation	Common in children who have SNI; can be an incidental finding rather than the source of pain: determine whether pain is associated with movement
Pressure sore	Increased risk in children unable to reposition and shift weight

children with neurological impairment that are attributed to "routine" problems (Carter, McArthur, and Cunliffe 2002; Hunt et al. 2004; Svedberg et al. 2008). Examples include teething, with an average pain intensity of 5.2 (0 to 10 scale) and duration of 18.5 hours, and constipation, with an average intensity of 6.2 and duration of 24.5 hours (Breau et al.

2003). Such findings suggest hyperalgesia resulting from neuropathic pain.

Peripheral neuropathic pain

Surgery appears to be a risk for the development of peripheral neuropathic pain. As an example, neuropathic pain was identified following orthopedic surgery in six children with cerebral palsy (Lauder and White 2005). Also suggesting this risk is the finding that children with SNI who have the highest pain ratings have the highest rate of surgical interventions (Hunt et al. 2007). In addition, persistent pain is reported in 10% to 50% of adults following common surgeries, becoming severe in 2% to 10% of these patients, with neuropathic pain considered an important cause of chronic postsurgical pain (Kehlet, Jensen, and Woolf 2006). Finally, some diseases of the nervous system may have associated painful peripheral neuropathy.

Central neuropathic pain

Central pain is another source of neuropathic pain (Frese et al. 2006; Nicholson 2004). It is observed in adults with injury to the CNS, such as from multiple sclerosis (MS) or following a cerebral vascular accident (stroke). Though historically called thalamic pain syndrome, it is not limited to injury of the thalamus (Klit, Finnerup, and Jensen 2009).

The symptoms experienced can be constant and can involve sudden bursts of intense pain. In addition to symptoms associated with nerve pain, such as burning and tingling, associated symptoms include visceral pain, experienced as painful fullness from normal distension of the GI tract and bladder—described by one adult as "like my bowels will explode" (Canavero and Bonicalzi 2007, 48). These symptoms associated with distension of the intestines may be relevant for children who have SNI, as discussed below. Though not described in children, central neuropathic pain is a likely source of pain behaviors in children with SNI.

Visceral hyperalgesia

Visceral hyperalgesia is an altered response to stimulation of the intestines, resulting in a decreased threshold for pain generation in response to a stimulus (Delgado-Aros and Camilleri 2005). As a result, a normal stimulus such as distension and pressure within the intestines, or minor tissue injury such as from GERD, can result in pain at a much lower level of

stimulation. This, along with central neuropathic pain with associated intestinal symptoms, is an important pain source to consider in children who have SNI.

These sources of pain are suggested by studies that identify the gut as one of the most common pain sources in children who have SNI, despite treatment of common causes of pain such as GERD and constipation (Breau et al. 2003, 2004; Carter, McArthur, and Cunliffe 2002; Houlihan et al. 2004; Hunt et al. 2003; Hunt et al. 2004). Pain attributed to the bowels is also noted to have a high pain intensity of 7.5 (0 to 10 scale), second only to pain of unknown cause (Breau et al. 2003). Other associations include significantly higher rates of pain in children already taking medications for GERD or gastrointestinal motility (Houlihan et al. 2004).

Nissen fundoplication and placement of a gastrostomy feeding tube (G tube) may also increase the risk of pain localized to the GI tract. Higher levels of pain, in response to the same degree of gastric distension, were identified in children after Nissen fundoplication (Mousa et al. 2006). In addition, parents of children who have SNI reported an increase in pain symptoms following placement of a G tube (Complex Child E-Magazine, neuro-crying, 2009).

For nonverbal children who have SNI, the following features may suggest visceral hyperalgesia, as well as the bowel symptoms associated with central neuropathic pain:

- Pain associated with G-tube feedings, suggesting a decrease in the threshold for generation of painful symptoms from normal gastric distension
- Pain associated with bowel gas and jejunostomy tube (J tube) feedings, suggesting pain associated with intestinal distension
- Pain associated with flatus (intestinal gas) and bowel movements, suggesting pain associated with distension of the colon
- Excessive response to a painful stimulus, such as prolonged crying spells associated with GERD.

When considering GERD as the source of pain, it is beneficial to review other, associated symptoms. As an example, when pain in children who have SNI is associated with retching, vomiting, and intolerance of tube feedings, other pain sources to consider include visceral hyperalgesia, stimulation of the vomiting reflex, and dysautonomia. These sources are reviewed in this chapter and in greater detail in chapters 5 and 7.

Problems that are sources of pain behaviors and are increased by other pain sources

Pain from any source can increase the features of other problems in children who have SNI. Examples include an increase in the frequency and severity of muscle spasms or an increase in the severity of features seen with autonomic dysfunction. In addition, these problems can also result in painful symptoms. Both are covered in greater detail in chapter 7.

Spasticity and muscle spasms

Impairment of the CNS can result in loss of voluntary control of muscles and the normal inhibitory control over muscle tone, resulting in the features of spasticity. Spasticity and muscle spasms can be increased by acute illness, discomfort, and pain. Spasticity is often not painful, but over time it can result in painful musculoskeletal injury. In addition, intense muscle spasms can result in intermittent pain.

Autonomic dysfunction

Autonomic dysfunction, also called dysautonomia, is becoming increasingly recognized in children who have SNI (Park et al. 2002; Svedberg et al. 2008). Other terms used for this condition include autonomic storm and sympathetic storm. Features that suggest dysautonomia include altered heart rate and body temperature; pale skin or flushing (redness) of the skin that often includes the face; retching, vomiting, and abdominal pain; abnormal sweating; and increased production of saliva (Axelrod and Berlin 2009; Chelimsky and Chelimsky 2001; Chelimsky, Hupertz, and Chelimsky 1999). Some features are the same as those associated with pain, including increased heart rate, pallor, sweating, stiffening, posturing, and agitation; others can contribute to discomfort, including abdominal pain and retching.

IN SUMMARY, spasticity and dysautonomia can contribute to discomfort, can have features also seen with pain, and can increase as a result of other pain sources. Treatment directed at spasticity and dysautonomia improves comfort in some children, and pain management diminishes the features of spasticity and dysautonomia in others.

Medication toxicity and withdrawal

There is significant overlap between pain behaviors and the features associated with medication toxicities or withdrawal symptoms (Bernard and Bruera 2000; Boyer and Shannon 2005; Jackson, Doherty, and Coulter 2008). This can include toxicity from a single drug, as well as toxicity from medication interactions. An example of the latter is starting a medication with an effect similar to that of one already in use, such as a second medication that can increase serotonin levels. In addition, toxicity or withdrawal symptoms can occur if a drug is started that can alter the metabolism of another medication.

Parents cannot feel responsible for knowing about every potential drug interaction or withdrawal, but they do need to consider whether any medication was changed in the weeks to months that preceded the start of symptoms. Information is summarized for healthcare providers in tables 4.2 and 4.3.

Medication toxicity

A place to start in considering medication toxicity is to review how long the features suggesting pain have been noted, then to identify whether any medication was started several months before these symptoms began. In general, medication categories to consider include the following:

- Dopamine antagonists (metoclopramide, risperidone)
- Benzodiazepines (clonazepam, diazepam, lorazepam, midazolam)
- Anticholinergics (glycopyrrolate, hyoscyamine, atropine, scopolamine, tricyclic antidepressant)
- Antihistamines (diphenhydramine, cyproheptadine)
- Selective serotonin reuptake inhibitors, SSRIs (citalopram, fluoxetine, sertraline)
- Serotonin-norepinephrine reuptake inhibitors, SNRIs (duloxetine, venlafaxine)

Though the features associated with medication toxicities can develop over hours to several days, there is often a significant delay in recognizing symptoms, especially in nonverbal individuals (Taddio and Oberlander 2006; van Maldegem et al. 2002). One study found that even adults able to report symptoms continued taking metoclopramide for an average of six

TABLE 4.2 Medication toxicities

Category	Associated features*	Potential causes (drugs commonly implicated or commonly used for children who have SNI)
Serotonin syndrome	*Increased heart rate and blood pressure*, *sweating*, hyperthermia, dilated pupils, diarrhea, *increased spasticity*, *clonus*, *agitation*	SSRIs and SNRIs; other drugs, often when used in combination: trazodone, risperidone, metoclopramide, linezolid, tramadol, fentanyl, TCA, ondansetron
Neuroleptic malignant syndrome	*Agitation*, *increased movement*, *muscle stiffening*, *autonomic dysfunction*, hyperthermia	Most commonly caused by dopamine antagonists (e.g., metoclopramide, haloperidol, risperidone)
Dystonic reactions, tardive dyskinesia	*Abnormal movement and posturing*, *agitation*	Dopamine antagonists (e.g., metoclopramide, haloperidol, risperidone)
Akathisia (unpleasant motor restlessness)	*Restlessness*, *distress*, tension, *discomfort*	Dopamine antagonists, TCAs, SSRIs, antihistamines; withdrawal from opioids and benzodiazepines
Agitation (unpleasant state of arousal)	*Increased movement*, *autonomic arousal* (sweating, increased heart rate), inability to relax	Paradoxical reactions to many medications, including anticholinergics, benzodiazepines, antihistamines, TCAs

*Behaviors associated with pain are in italic.

months after the start of involuntary movements associated with tardive dyskinesia (Miller and Jankovic 1989). Symptoms can also be nonspecific, such as irritability identified as the most common side effect in infants treated with metoclopramide (Hibbs and Lorch 2006). The features associated with specific drug toxicities are outlined in table 4.2.

Medication withdrawal

Medication withdrawal, when a medication is stopped abruptly or discontinued too quickly, can also result in pain symptoms (Ducharme et al.

2005; Fisher 2010; Franck, Naughton, and Winter 2004). This change in status can create a false assumption that the medication was treating a problem and therefore was providing benefit. The withdrawal features associated with specific medications are outlined in table 4.3. In general, medication withdrawal can result in symptoms in three categories:

1. Excitation of the CNS, with agitation, restlessness, and muscle spasms
2. Activation of the sympathetic nervous system, with increased heart rate, blood pressure, and sweating
3. Gastrointestinal symptoms such as cramps, vomiting, and diarrhea

Withdrawal symptoms can be minimized by providing an appropriate taper schedule for the medication and by monitoring for symptoms that suggest withdrawal. The risk of withdrawal symptoms and duration of tapering depend on the medication and duration of use. In general, baclofen, clonidine, and gabapentin can be tapered over 2 to 4 weeks, such as decreasing by 10% to 20% every 2 to 3 days, whereas benzodiazepines, opioids, tricyclic antidepressants (TCAs), and SNRIs often require longer tapering, sometimes over 4 to 12 weeks. Information from studies includes the following points:

- Patients taking long-term oral benzodiazepine benefit from a taper over 8 to 12 weeks, decreasing every 7 days by an amount that is

TABLE 4.3 Medication withdrawal symptoms

Drug category	Features
Opioids	Agitation, restlessness, grimacing, inconsolable crying, disrupted sleep, hiccups, goose bumps, shivering, fever, increased heart rate and blood pressure, increased respiratory rate, vomiting, gagging, diarrhea, cramps, tears, runny nose, yawning, sweating, dilated pupils, muscle spasms, seizures
Benzodiazepines	Jitteriness, agitation, increased heart rate, muscle cramps, disrupted sleep, heightened sensitivity to light and sound
Baclofen	Agitation, confusion, hallucinations, insomnia, hyperthermia, seizures, rebound spasticity, muscle rigidity
TCAs and SNRIs	Agitation, irritability, disrupted sleep, GI distress, tremor, sweating

10% of the initial dose, though some patients may need a longer taper (Lader, Tylee, and Donoghue 2009).
- TCA and SNRI doses can be lowered every 5 to 7 days over a minimum of 2 weeks, though more often over 4 to 12 weeks (Shelton 2001).
- *Most important:* (1) Monitor for withdrawal symptoms and adjust the wean schedule as needed, (2) consider other sources of the symptoms identified, and (3) recognize that there can be more harm from tapering too quickly than from tapering too slowly.

Two or more sources of pain may coexist

Children who have SNI are at risk for several sources of pain occurring simultaneously, an important consideration when determining treatment and follow-up plans. As an example, a child may have GERD as well as visceral hyperalgesia and/or central neuropathic pain. This combination may be evident only after symptoms improve somewhat, yet may remain troublesome despite the treatment of GERD. This combination may also be suspected when symptoms are out of proportion to the problem, such as prolonged and severe crying associated with teething in a child with central pain. It is also important to consider other causes of pain behaviors when problems such as spasticity and autonomic dysfunction remain resistant to treatment.

When more than one source of pain is addressed, children may experience earlier symptom improvement with empirical treatment of neuropathic sources along with treatment of nociceptive sources. The sources to be considered are summarized in table 4.4.

THE QUESTIONS in table 4.5 can assist in the process of prioritizing potential sources of pain when pain behaviors are identified in a child who has SNI.

AN APPROACH TO PAIN TREATMENT

Pain treatment starts with an assessment for sources of pain, as outlined in table 4.1 and figures 4.1 and 4.2, which then allows treatment and elimination of the sources. This includes treating problems that are common in children who have SNI and may contribute to discomfort, such as constipation, GERD, and spasticity.

TABLE 4.4 Summary of pain sources to consider in children who have SNI

Source	Comments
Nociceptive pain	• A normal and expected response to injury and inflammation of tissue in the body • Causes to consider: GERD, bladder infection, kidney stones, gallstones, bone fracture, pancreatitis (inflammation of the pancreas), dental problems, hip subluxation (table 4.1)
Drug toxicity or withdrawal	• Review when the features that suggest pain started and whether any medication was started or stopped prior to the onset of these features, including starting a drug with the same mechanism of action as another drug being used, or one that can alter the metabolism of other drugs • Medications with side effects that are similar to the features associated with pain: metoclopramide (Reglan), benzodiazepines, anticholinergics (table 4.2) • Medications that can result in withdrawal symptoms: benzodiazepines, baclofen, TCAs, opioids (table 4.3)
Neuropathic pain	• A result of nerve damage • Associated with surgery, such as surgery of the lower extremities or of the spine
Central pain	• A result of damage or dysfunction of the brain; specifically, the areas in the CNS that receive and process input about pain and touch • Symptoms can include constant pain, sudden bursts of intense pain, and painful symptoms from distension of the stomach, intestinal tract, or bladder
Visceral hyperalgesia	• Increased sensitivity to stimulation in the GI tract, such as a painful response to distension of the stomach or bowels, or an exaggerated pain response to tissue injury such as from GERD • Can develop following Nissen fundoplication or other surgery to the GI tract
Autonomic dysfunction (dysautonomia)	• Some features associated with autonomic dysfunction are also associated with pain: sweating, flushing (red skin), increased heart rate, agitation, and stiffening • Important to consider pain as a trigger for autonomic "storms"
Spasticity	• Muscle spasms can be painful • Spasticity is often not painful but can result in musculoskeletal pain

TABLE 4.4 *(continued)*

Source	Comments
	• Other pain sources can be a trigger for increased tone and muscle spasms
Two or more pain sources may coexist	• Important to consider when no pain source is identified or when pain behaviors continue despite treatment of identified sources; for example, consider central neuropathic pain or visceral hyperalgesia when GI symptoms persist despite treatment of GERD

Neuropathic pain, central pain, and visceral hyperalgesia are also important to consider, as they may be the primary reason for the observed pain behaviors or may cause an increased pain response from a known pain source. For example, it is beneficial to consider these causes of pain when a child with teething, GERD, intestinal gas, or constipation has prolonged and severe crying spells that seem out of proportion to the problem. Some children benefit from treatment of a contributing nociceptive source along with a medication trial directed at neuropathic pain / central pain / visceral hyperalgesia.

It is not necessary to obtain every test for all possible causes of nociceptive pain before initiating an empirical medication trial for such sources as central pain. This approach to testing could both delay the initiation of a medication that might target the source of a symptom and put a child through potentially unnecessary tests. There are no hard and fast rules. Instead, it can be helpful to consider some of the following questions:

- What will be learned from the test?
- What discomfort or harm can be caused by the test?
- What will be done with the information obtained from the test?
- How will the treatment plan be altered by the test?
- What is the risk associated with the medical or surgical intervention?
- Has there been an empirical medication trial directed at pain sources that can trigger such problems as spasticity and GI symptoms, including pain and vomiting?

To illustrate this process, consider a child with persistent pain associated with the bowels, with negative findings on tests for sources important

TABLE 4.5 A child's history as a guide to sources of pain behaviors

Questions	Reason/type of pain indicated
Does your child become agitated or appear to be in distress? Do you have any worries about your child being uncomfortable or in pain?	Identify presence of pain/pain behaviors
What do you notice in your child when she appears uncomfortable? Are there times when her face appears distressed or when she becomes more withdrawn? Does her body stiffen or arch? Are there unusual responses such as hitting her face or laughing but not seeming happy?	Identify specific pain behaviors
How does this compare with other times when you have seen your child in pain? How would you rate this pain on a scale of 1-10, with 1 being minimal pain and 10 being the worst you have seen or could imagine in your child? How often and for how long are pain symptoms occurring?	Identify severity, frequency, and duration of symptoms
Does your child have problems with tube feedings, retching, gas, or constipation that make him uncomfortable? Does he have muscle spasms, dystonia, or autonomic storms that appear distressing and uncomfortable?	Identify problems that can increase in severity as a result of pain and yet are not typically thought of as indicating "pain"
How well does your child sleep? When she wakes at night, is she usually comfortable or uncomfortable?	Sleep can be disrupted by pain
Were any medications started or stopped in the weeks to months before noticing these symptoms?	Drug toxicity or withdrawal
Does your child have a dislocated (subluxed) hip? If so, is pain associated with movement of the legs, such as with transfers, clothing, diapering, and repositioning?	Determine whether the dislocated hip is a source of pain or an incidental finding without associated pain
Does your child continue to have discomfort despite treatment of painful problems, such as gastroesophageal reflux?	Identify coexisting central pain, visceral hyperalgesia
Did your child have any surgery before the onset of these symptoms, such as feeding tube placement, Nissen fundoplication, or orthopedic surgery?	Postsurgical neuropathic pain or visceral hyperalgesia
Does your child experience recurrent episodes of intense and rapid-onset pain, crying, and stiffening that seem to occur "out of the blue"?	Sudden bursts of intense pain as described with central pain

TABLE 4.5 *(continued)*

Questions	Reason/type of pain indicated
Are you able to locate the area of pain? Do you suspect it is related to the gut?	Visceral hyperalgesia or central pain
Is there pain associated with tube feedings, with intestinal gas, or prior to a bowel movement? Does the pain decrease after venting the G tube, when passing gas, or after a bowel movement? Is there associated retching?	Visceral hyperalgesia or central pain
Does your child have any of the following features occurring together: sweating, flushing of the face or other areas of the body, increased heart rate, increased temperature, retching or gagging, back arching?	Autonomic dysfunction
Do you think your child is in pain before becoming stiff or having muscle spasms? Does your child have persistent problems with episodes of recurrent muscle spasms, stiffening, and arching despite the use of medications for spasticity?	Pain as a trigger for muscle spasms

to consider, such as pancreatitis, UTI, and gallstones. If the child has persistent pain behaviors despite treatment for GERD, further testing could include an upper gastrointestinal series (UGI), pH probe, or upper endoscopy of the esophagus and stomach. On the other hand, gabapentin may be a reasonable next step, given the similarities in symptoms between GERD and visceral hyperalgesia / central pain, as well as the safety of such a medication trial. If improvement occurs, the child will have avoided further testing and interventions for GERD, including surgery. Ideally, both parents and physicians have full knowledge of these available options and approaches; everyone's comfort with the process is improved when there is maximal knowledge of the risks and benefits of different approaches.

A guide to obtaining tests and initiating an empirical medication trial

It helps to consider separately the child who has new, acute pain and the child with pain behaviors that continue despite a search for causes and treatment of identified problems. For the child with new-onset pain, table

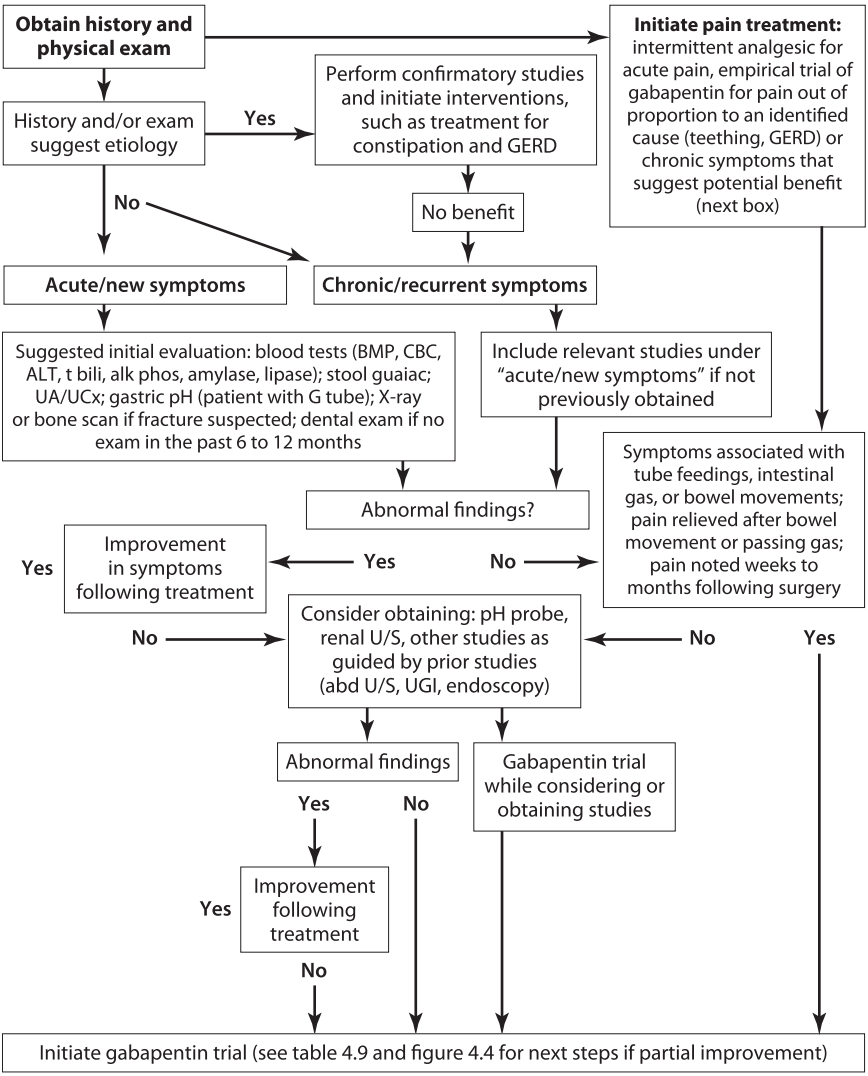

Obtain history and physical exam
Initiate pain treatment: intermittent analgesic for acute pain, empirical trial of gabapentin for pain out of proportion to an identified cause (teething, GERD) or chronic symptoms that suggest potential benefit (next box)
History and/or exam suggest etiology
Yes
Perform confirmatory studies and initiate interventions, such as treatment for constipation and GERD
No
No benefit
Acute/new symptoms
Chronic/recurrent symptoms
Suggested initial evaluation: blood tests (BMP, CBC, ALT, t bili, alk phos, amylase, lipase); stool guaiac; UA/UCx; gastric pH (patient with G tube); X-ray or bone scan if fracture suspected; dental exam if no exam in the past 6 to 12 months
Include relevant studies under "acute/new symptoms" if not previously obtained
Symptoms associated with tube feedings, intestinal gas, or bowel movements; pain relieved after bowel movement or passing gas; pain noted weeks to months following surgery
Abnormal findings?
Yes
Improvement in symptoms following treatment
Yes
No
No
Consider obtaining: pH probe, renal U/S, other studies as guided by prior studies (abd U/S, UGI, endoscopy)
No
No
Yes
Abnormal findings
Gabapentin trial while considering or obtaining studies
Yes
No
Yes
Improvement following treatment
No
Initiate gabapentin trial (see table 4.9 and figure 4.4 for next steps if partial improvement)

Figure 4.2. Algorithm for pain/irritability. *Abbreviations:* abd U/S, abdominal ultrasound; alk phos, alkaline phosphatase; ALT, alanine aminotransferase; BMP, basic metabolic panel; CBC, complete blood count; GERD, gastroesophageal reflux disease; t bili, total bilirubin; UA, urine analysis; UCx, urine culture; UGI, upper gastrointestinal series; U/S, ultrasound.

4.1 serves as a guide to the problems to consider. After obtaining a history and physical exam, the physician will consider which diagnostic tests to obtain, as shown in figure 4.2. This is often the time when blood and urine tests are ordered, to determine whether a child has a bladder infection, pancreatitis, or other acute problems that could explain the acute onset of

pain. X-rays of limbs might be obtained, if the symptoms are brought on by movement or if swelling is noticed on physical examination, given the increased risk of bone fractures in children who are unable to bear weight and walk. In addition, empirical treatment of GERD is often initiated at this time. This may include giving an antacid to see whether symptoms decrease, while also starting a medication to decrease acid production in the stomach, such as ranitidine (Zantac) or omeprazole (Prilosec).

More challenging is the child with no identified source of pain or continued pain behaviors despite treatment of such problems as GERD. This can understandably leave a parent fearful that more tests need to be obtained until the cause can be identified. Though it is important to consider further studies, this is also a time to consider a pain treatment trial. This reflects the risk of there being pain sources that will not be identified by tests, such as central or peripheral neuropathic pain; furthermore, some tests are not readily available and are invasive to complete, such as barostat testing for visceral hyperalgesia. Improvement following a medication trial directed at such problems as central neuropathic pain and visceral hyperalgesia can also be an indirect indicator of the source of pain. Finally, in some cases, empirical trials can be beneficial before pursuing surgical interventions for certain problems, such as Nissen fundoplication for GERD (discussed in chapter 5) or an intrathecal baclofen (ITB) pump for persistent and severe spasticity (discussed in chapter 7). Such surgical interventions can be beneficial, yet some children will benefit from empirical medication trials that decrease or eliminate the problem that the surgery is intended to treat.

The importance of nonpharmacological interventions

Nonpharmacological interventions, also referred to as integrative management and complementary alternative therapies, are an essential part of symptom management strategies. It is beneficial to incorporate such strategies along with the medical options.

Parents of children who have SNI become adept at identifying comfort strategies such as cuddling, rocking, massaging, and repositioning. Other methods that can benefit some children include warm baths, swaddling, weighted blankets, and music with headphones. For persistent muscle spasms that include stiffening of the arms and legs, some parents report benefit from bringing the head forward so that the chin is closer to the chest to break the spasm. Other interventions for consideration, though not studied in these children, include aromatherapy and acupuncture (Liptak 2005).

Supportive equipment such as seating systems and supportive pillows can minimize positional pain. Vibratory stimulation is reported in the literature as beneficial for chronic pain, and a parent has reported it to be beneficial for her child who has SNI (Complex Child E-Magazine, vibration, 2009; Lundeberg 1984; Lundeberg et al. 1987). The benefit of vibratory stimulation is also suggested by the frequency with which parents report how much their child "loves" and is "happy" when the vibratory pulmonary vest is used to assist with mucus mobilization. Products available include vibrating mats and pillows. Physical therapists and social workers can assist with identifying equipment options or identifying a vendor for equipment needs.

For symptoms localized to the intestinal tract, strategies include venting of a G tube, use of equipment that allows venting during feedings (such as the Farrell valve bag pressure relief system), and slower tube feedings. In addition, a decrease in the total volume of fluids given by feeding tube will benefit some children, as a result of less distension of the stomach and intestines.

Ben is a 6-year-old who has SNI as a result of a metabolic disease, with some discomfort associated with his G-tube feedings. He is described as "so much more comfortable" after the amount of water given each day is dropped from 1,000 mL to 500 mL, yet the parents feel it took a "standoff" to get agreement from the dietician and medical specialists. Ben continues to do well on his 500 mL of water.

Jarred is a 3-year-old who has SNI as a result of a hypoxic event at 2 years of age. His comfort is improved by more than 75% with the use of gabapentin, which decreases the frequency, severity, and duration of crying spells. Associated features include facial flushing, increased secretions, increased heart rate, and stiffening of his extremities. Though episodes are now infrequent and less severe, when they do occur, Jarred benefits from use of a vibratory mat. When the mat is used, he becomes quiet and calm, usually not requiring an analgesic for breakthrough pain.

Empirical treatment of pain and sources of pain behaviors

When pain behaviors persist despite treatment of an identified source, or when pain appears to be out of proportion to the source, or when no source is found, children who have SNI often benefit from a medication

trial that targets neuropathic pain, central pain, and visceral hyperalgesia. In addition, empirical treatment for these problems can be initiated while considering further testing for nociceptive sources (figure 4.2). Improvement with an empirical medication trial for central pain / visceral hyperalgesia / neuropathic pain provides indirect evidence that a potential source has been treated.

Central pain, visceral hyperalgesia, and neuropathic pain

The best-studied medications for these pain sources are TCAs (such as nortriptyline), gabapentin, and pregabalin (Berde, Lebel, and Olsson 2003; Dworkin et al. 2007; Finnerup et al. 2005; Frese et al. 2006; Hasler 2003; Houghton et al. 2007; Klit, Finnerup, and Jensen 2009; Lee, Kim, and Cho 2005; Nicholson 2004; Zangen et al. 2003). Other medications used for adults with neuropathic and central pain include SNRIs (duloxetine, venlafaxine), anticonvulsants (valproic acid, carbamazepine, lamotrigine), opioids, *N*-methyl-D-aspartate (NMDA) receptor antagonists, and cannabinoids. One must be cautious when using interventions that have not been studied in children, though studies in adults do provide a theoretical basis for considering these medications for children who have SNI.

Spasticity

For generalized spasticity that may be contributing to pain, treatment recommendations published in 2010 include diazepam, recommended only for short-term use, and tizanidine, with less evidence regarding its benefit (Delgado et al. 2010). Baclofen, clonidine, and dantrolene may offer benefit for some children, though there is insufficient evidence that one provides greater benefit over another. Gabapentin may also be beneficial for some children, but this has been studied best in adults with MS (Cutter et al. 2000). For spasticity that is more localized, botulinum toxin type A (Botox) is both effective and safe in reducing spasticity in children with cerebral palsy, as well as reducing associated pain (Delgado et al. 2010; Lundy, Doherty, and Fairhurst 2009; Rivard, Nugent, and Symons 2009). ITB is another option for treatment of generalized spasticity that remains significant following other treatments.

When considering a medication for pain and associated spasticity in a child who has SNI, one should also take note of the other beneficial properties of medications used for spasticity. As an example, tizanidine and clonidine, alpha-2 receptor agonists, may have mild antinociceptive

properties through substance P modulation (Semenchuk and Sherman 2000; H. Smith and Elliott 2001). Of the options, clonidine and gabapentin may be preferred in treating spasticity in children with SNI when there is difficulty distinguishing whether pain or spasticity is the primary problem. Both drugs have been studied in children and have the convenience of liquid formulation, as well as a transdermal patch for clonidine.

Autonomic dysfunction

Evidence regarding treatment of autonomic dysfunction is limited to case reports, predominantly of patients with brain injury as a result of trauma or lack of oxygen. Medications include clonidine, benzodiazepines, cyproheptadine, morphine sulfate, bromocriptine, oral and intrathecal baclofen, and beta antagonists (Axelrod and Berlin 2009; Baguley 2008; Baguley et al. 2004; Diesing and Wijdicks 2006). No study identifies one medication as more beneficial than another. Case reports suggest that cyproheptadine may be beneficial for patients with associated retching and vomiting or with associated hypothermia (Kloos 1995; Ruiz et al. 2003; Sheth, Barron, and Hartlage 1994). Finally, two recent studies found that gabapentin and pregabalin are beneficial in treating autonomic dysfunction, expanding the potential utility of these medications (Axelrod and Berlin 2009; Baguley et al. 2007).

As in the case of spasticity, it is useful to consider other properties when making decisions on medications for autonomic dysfunction, especially for the child with associated pain behaviors. There may be a preferential role for gabapentin, pregabalin, and clonidine, given the difficulty in distinguishing whether pain or autonomic dysfunction is the primary problem. Along with the use of a scheduled medication (such as gabapentin, clonidine, or cyproheptadine, depending on associated features), children with intermittent autonomic storms can benefit from as-needed (prn) clonidine, morphine, or benzodiazepine during pain episodes.

Gabapentin and tricyclic antidepressants

Gabapentin has a good safety profile in children, including no known drug-drug interactions, making it a safe first choice for an empirical trial for patients with persistent symptoms. As an example of benefit, nine children with SNI who were treated with gabapentin experienced a significant reduction in pain symptoms, as well as improvement in feeding tolerance and sleep (Hauer, Wical, and Charnas 2007). Problems that may benefit

from gabapentin include visceral hyperalgesia, central pain, spasticity, and autonomic dysfunction.

Gabapentin is known to be safe for children at doses of up to 78 mg/kg/day, with children younger than 5 years of age requiring the higher dose (Haig et al. 2001; Korn-Merker, Borusiak, and Boenigk 2000). Pregabalin is another option; it has higher oral bioavailability than gabapentin (90% vs. 33% to 66%), with a linear increase in plasma concentration with increasing doses, compared with gabapentin's decreasing bioavailability at higher doses. There are no data to indicate that this results in a greater clinical benefit for children.

Whether children and adults who have SNI are more likely to benefit from gabapentin or from a TCA such as nortriptyline is not yet known. Until there is further information to indicate when one might be preferred over the other, gabapentin is suggested as a first-line medication; it is generally safer, with fewer significant side effects than TCAs and no known interactions with other drugs.

As with many of the medications reviewed here, the literature on adults guides the consideration of medications for problems in children who have SNI. Yet one clearly must be cautious when interpreting this information; for example, there is a greater likelihood that central neuropathic pain contributes to symptoms in children who have SNI, yet less evidence to guide the treatment of central pain. The literature on treatment of adult "neuropathic pain" is typically focused on peripheral neuropathic pain resulting from such conditions as diabetic neuropathy. In addition, the number needed to treat (NNT—a number used to compare the relative benefit of one treatment over another) identified for gabapentin varies, depending on the dose used in different studies. As an example, a much more favorable NNT was identified when studies using a total of 900 mg or less per day were excluded, a dose that is equivalent to only 18 mg/kg/day or less in children (Finnerup et al. 2005).

For children who have partial benefit from gabapentin, the addition of nortriptyline may be useful. This is supported by one study that identified greater benefit with this combination for treating neuropathic pain in adults than with either medication alone (Gilron et al. 2009).

Clonidine and tizanidine

As reviewed earlier, clonidine is used in the treatment of spasticity and autonomic dysfunction, and tizanidine in the treatment of spasticity. In addition, both have potential mild antinociceptive properties through substance

P modulation. There is also limited information that suggests the benefit of clonidine in reducing pain perception during gastric and colonic distension (Kuiken, Tytgat, and Boeckxstaens 2005). The side effects, such as low blood pressure and sedation, are infrequent and can be minimized by starting with one dose a day, with an increase every 3 to 4 days, as tolerated.

Nonsteroidal anti-inflammatory drugs and acetaminophen

Pain medications that are used for mild pain include acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen (see figure 4.3). They have an important role in symptom relief for children who have SNI. Invariably, such medications have already been tried when a child with SNI is experiencing persistent pain behaviors. When such a medication is not providing symptom relief for the child, it is indirectly indicating that the problem is more significant than a routine ache or pain. This then suggests two important considerations: pain that is excessive for the problem (hyperalgesia) and the need to utilize more effective pain treatment.

The World Health Organization pain ladder

The World Health Organization (WHO) pain ladder provides general guidelines for selecting medications, based on whether the pain is mild, moderate, or severe (figure 4.3). If a pain medication in one category is not effective, a pain medication from the next step of the ladder can be selected. Given the challenge of categorizing the degree of pain in a child who has SNI, this latter point is an important part of selecting a pain medication. It is also important to be circumspect about using the WHO

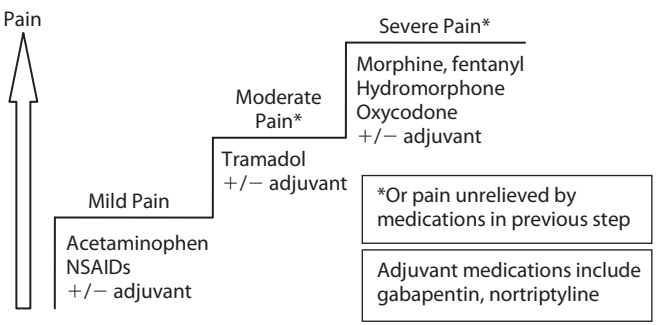


Figure 4.3. World Health Organization pain management ladder

pain ladder when treating pain in children who have SNI, because it was developed for patients with cancer (though the same principles apply).

When pain does not improve with a medication from the first step of the pain ladder, indicated as mild pain, medications from the second and third steps need to be considered. It also helps to recognize the role of adjuvant medications, as indicated at each step of the pain ladder. Adjuvant medications are medications that can provide independent benefit for specific types of pain, such as neuropathic pain, or can enhance the benefit of other medications used for pain treatment. Gabapentin and nortriptyline are examples of adjuvant therapies. They may have a preferential role for children who have SNI, before the use of an opioid, given their utility in treating the specific types of pain for which such children are at risk.

A proposed alternative to the WHO pain ladder is provided at the end of the chapter, in recognition of the differences between children with SNI and patients with cancer (see figure 4.4). Some of these differences are (1) children who have SNI are much more likely to have pain behaviors resulting from abnormalities in the nervous system (central neuropathic pain, visceral hyperalgesia, autonomic storms, muscle spasms); (2) these children are less likely to have chronic nociceptive pain; and (3) it can be more difficult to rate pain in categories of mild, moderate, and severe in such children.

Other details about medication selection

- *NSAIDs and acetaminophen can be used* along with an adjuvant medication and with opioids when treating moderate to severe pain.
- *Tramadol is effective for moderate pain*, but must be used with caution for patients with a seizure disorder, for patients taking medications that are inhibitors of cytochrome P450 2D6 isoenzyme, such as TCAs and metoclopramide, and for patients taking medications that are associated with serotonin syndrome, as indicated in table 4.2 (Boyer and Shannon 2005; Gardner et al. 2000).
- *Codeine is not recommended* when other medications are available, because it is ineffective in up to one-third of individuals as a result of their inability to metabolize codeine to the active metabolite morphine, and it can result in toxicity in individuals who are ultrarapid metabolizers (Ciszkowski et al. 2009; Williams, Patel, and Howard 2002).
- *Meperidine is not recommended*, because its metabolite can result in seizures, especially with long-term use.

- *Fentanyl and methadone are the safest opioids for individuals with renal failure* (Dean 2004; Murphy 2005).

Opioids for pain treatment

For children who have SNI, opioids are most commonly used as needed (prn) for intermittent symptoms. This may include management of acute nociceptive pain, such as postsurgical pain or pain resulting from a bone fracture; for acute breakthrough pain that occurs despite the use of scheduled medications such as gabapentin; and as an option for intermittent autonomic storms and dyspnea. When an oral opioid is used, the benefit is typically noted within 15 to 30 minutes, with peak onset at 1 hour and duration of 3 to 4 hours. When a starting dose of an opioid is not providing pain relief, the dose can be increased by 30% to 50% per day for continued moderate pain. If pain remains severe, it may be necessary to increase the opioid dose by 50% to 100%.

If an opioid is the only medication being used for chronic, daily pain, it should be scheduled around the clock (ATC) based on the duration of benefit of the opioid, typically every 4 hours when given orally (G tube). When an opioid is scheduled ATC and given every 4 hours, the as-needed dose for breakthrough pain is 10% of the total 24-hour opioid use, available as often as every 1 to 2 hours for the oral form.

For children unable to swallow medications, methadone is the only opioid that provides pain relief for longer than 4 hours that is available in a liquid form to be given by G tube. (More information on this is provided later in the chapter.) The fentanyl transdermal patch is the other option for continuous ATC opioid dosing. The fentanyl patch should be initiated only after determining the ATC opioid dose that is sufficient for pain control. A 12 μg patch, the lowest available fentanyl patch dose, is equivalent to approximately 25 mg of oral morphine per day.

There are times when a switch from one opioid to another is beneficial, such as when side effects persist. A dose that provides equivalent pain relief can be calculated when changing from one opioid to another. The calculated equivalent dose must be decreased by 25% to 50% to avoid overmedication. This is known as cross-tolerance and reflects differences in the structure and binding of each opioid to the receptors that transmit pain. For pain that is well controlled, the decrease should be closer to 50% of the calculated dose, and for pain that remains mild to moderate, the decrease should be closer to 25%.

Common fears about the use of opioid medications include fear of doing harm, fear of drug addiction, and fear of giving up too soon. It is helpful to understand that drug dependence with chronic use of an opioid is different from drug addiction. *Physical dependence* refers to the need to slowly taper a medication so as to avoid withdrawal symptoms from a sudden stop or reduction in the medication's dose. In contrast, *drug addiction* refers to a psychological desire for and dependence on a drug.

The association of opioid use with end-of-life care can lead to the assumption that opioids either hasten death or indicate that someone is dying, when he or she is not. When used appropriately, opioids do not hasten death but can ensure comfort throughout life. In addition, more recent evidence suggests that patients who receive attention to symptom management may have a prolonged survival, due to reduced physical and psychological stress and exhaustion (Temel et al. 2010).

Fear about development of respiratory depression, with a decrease in the rate and effort of breathing, is one of the greatest barriers to the use of opioids, including at the end of life. This is an unwarranted fear, as opioid-induced respiratory depression is unlikely with appropriate dosing and titration. The initial starting dose can be lowered from the routine starting dose for a patient with compromised breathing, a decreased level of alertness, or a history of oversedation from a routine starting dose. The dose can then be increased in a standardized manner until pain is adequately treated. When morphine is used for dyspnea, the starting dose is 25% to 30% of the starting dose used for pain. Physicians with training in pain and palliative care can provide guidance on how to effectively and safely increase the dose if the initial dose is not adequate.

When opioids are used over the long term, side effects need to be anticipated and managed as they occur. The most common side effect is constipation, which should be managed proactively by initiating treatment or by increasing any treatment for current constipation. Table 4.6 summarizes further information about side effects associated with opioids.

Methadone

Methadone is the only long-acting opioid available as a liquid—a benefit for children with a feeding tube. Methadone can provide continuous pain relief with a dose given either every 8 or every 12 hours. In contrast, other opioids available as a liquid provide pain relief for 3 to 4 hours. In addition to having the same mechanism of action as other opioids (mu-opioid

TABLE 4.6 Management of opioid side effects

General approach for all side effects

- Monitoring over several days for improvement of mild symptoms, such as sedation and nausea, without any changes in dosing
- Management of side effects (see below)
- Dose reduction of the opioid (preferably *only* if good pain control)
- Opioid rotation (switching to a different opioid)

Respiratory depression

- Breathing often less labored with pain control; significant opioid-induced respiratory depression is unlikely with appropriate dosing
- Risk factors: renal impairment; other causes of depressed breathing, including medications; patients whose pain has resolved

Sedation that persists (though typically improves)

- Discontinue less necessary drugs that can cause sedation

Constipation

- Laxatives required with opioid use
- Start with a stimulant (senna) and stool softener (docusate)
- Other options include Miralax or lactulose

Urinary retention

- Bladder catheterization

Nausea and vomiting

- Usually improves after several days
- Antiemetic, either scheduled or as needed

Itching (pruritus)

- Antihistamines typically not effective, because opioid-induced itching is not mediated by histamine

Myoclonus (usually with higher doses)

- Clonazepam

agonist), methadone may have added utility for treating neuropathic pain (Moulin et al. 2005): it is an NMDA receptor antagonist against glutamate, which is an excitatory neurotransmitter in the brain.

The challenges with using methadone are due to its two-phase elimination from the body and the effect of other medications on its metabolism.

The unique metabolism of methadone as a result of this biphasic elimination can result in drug accumulation and toxicity 2 to 5 days after starting or increasing the drug (Bruera and Sweeney 2002; Strouse 2009). For this reason, methadone use requires expertise from the healthcare provider. Potential drug interactions that may be relevant for children who have SNI include the following (this is a partial list of drugs commonly used for such children):

- Medications that decrease the effect of methadone by increasing metabolism (or increase the effect when discontinued): phenobarbital, phenytoin, carbamazepine, risperidone
- Medications that increase the effect of methadone by decreasing metabolism: ciprofloxacin, diazepam, metronidazole, erythromycin
- Medications that increase the risk of QT prolongation: TCAs, phenothiazines, neuroleptics, levofloxacin

Benzodiazepines

A few comments about benzodiazepines are warranted here, because they are commonly used to treat persistent irritability and agitation in children who have SNI. Other reasons for their use include spasticity, dystonia, dysautonomia, seizures, and sleep problems. Diazepam, midazolam, lorazepam, and clonazepam are examples of commonly used benzodiazepines. They are generally safe and effective in the short term, although sedation and paradoxical effects such as increased agitation and irritability can occur (Kalachnik et al. 2002, 2003).

Daily, prolonged use results in tolerance due to a decrease in the benzodiazepine binding sites, requiring an increase in dose to provide the same level of benefit. Increasing the dose as tolerance develops may carry a risk of side effects that outweighs the intended benefit of the daily medication. As the dose is gradually increased over time, it can become difficult to separate potential side effects, such as agitation and irritability, from the effects of the neurological disease or of other medications. Here are some details about these benzodiazepines:

- *Midazolam, diazepam, and clonazepam—drug-drug interactions:* The effects of these medications can be altered by other medications, because they are metabolized by the P450 enzyme system. This can result in altered metabolism caused by enzyme inhibitors such as

erythromycin, ciprofloxacin, and antifungals (fluconazole, ketoconazole) and by enzyme inducers such as phenobarbital, phenytoin, and carbamazepine (Devlin and Roberts 2009; Riss et al. 2008; Tanaka 1999).

- *Lorazepam does not undergo these drug-drug interactions:* Because it is metabolized by conjugation, lorazepam is not altered by the medications noted above.
- *Midazolam—advantage of more rapid onset:* Midazolam is highly fat soluble, which results in a rapid distribution into the brain and fat tissues and thus a more rapid onset of action. This can be an advantage for intermittent acute symptom management.
- *Midazolam—disadvantage of accumulation:* As a result of this high fat solubility, daily use for intermittent symptoms or continuous use (intravenous or subcutaneous) can lead to accumulation (Gan 2006). There may be a continued effect once stopped, given its prolonged elimination with continuous use and its high fat solubility, which can lead to accumulation in the body. This is relevant for children who have SNI, because body measurements such as weight can underestimate the percentage of body fat in such children (Kong and Wong 2005; Kuperminc et al. 2010).
- *Clonazepam—risk of increased secretions:* Clonazepam can result in significant saliva production and bronchial secretions in some patients, possibly a greater risk in younger children (Browne 1976, 1978).

Ideally, long-term daily use of benzodiazepines is limited. There are times when the benefit of daily use may outweigh the disadvantage of tolerance and other concerns, such as the use of clonazepam for certain seizure types. For other indications, benzodiazepines are best used intermittently, such as for intermittent muscle spasms, autonomic storms, or prolonged seizures. The other option is short-term use, for less than 2 to 4 weeks, as other medications such as gabapentin, nortriptyline, or clonidine are initiated. This includes the recommendation that diazepam be used as a short-term treatment of spasticity in cerebral palsy (Delgado et al. 2010). One case series identified clonazepam as having a potential benefit for neuropathic pain in cancer patients, though treatment was of short duration (Hugel, Ellershaw, and Dickman 2003). Whether the benefit would have declined with longer use as a result of tolerance to the medication is unknown.

Sudden cessation after prolonged use of a benzodiazepine can result in a withdrawal syndrome, producing such symptoms as jitteriness, agitation, anxiety, increased heart rate, muscle cramps, disrupted sleep, GI upset, and heightened sensitivity to light and sound. When benzodiazepines are used intermittently, it is important to monitor for "intermittent" use that becomes daily—another scenario in which withdrawal symptoms can occur. One review of benzodiazepine tapering after long-term use suggested a taper over 8 to 12 weeks, such as decreasing the dose by no more than 10% every week. Some patients may need a longer taper, recommended to be no longer than 6 months (Lader, Tylee, and Donoghue 2009).

Sondra is a 4-year-old girl who has SNI as a result of non-accidental trauma as an infant. Her clonazepam treatment was recently tapered, as it was unclear whether it was still needed. Sondra is described as being comfortable and quiet at that time; there were no concerns about sleep. For Sondra's first week without clonazepam, her family was delighted to see her much more awake and interactive. One week later, Sondra became progressively more irritable and stiff. Her mother said, "I think this is why she was started on this medication in the first place." She is now concerned that for Sondra to be comfortable she must also be sedated. Two considerations are discussed: the option of initiating gabapentin or nortriptyline and the possibility that these symptoms are a result of withdrawal. Gabapentin is started, with the hope that a different medication will allow Sondra to be comfortable without being sedated. Her comfort improves significantly, with Sondra remaining awake and alert.

Serotonin-norepinephrine reuptake inhibitors

Serotonin-norepinephrine reuptake inhibitors are considered first- or second-line therapy for adults with neuropathic pain (Dworkin et al. 2007; Moulin, Clark, and Gilron 2007). The SNRIs include venlafaxine and duloxetine. Most studies have involved adult patients with peripheral neuropathic pain, with less information to support the benefit of SNRIs for central pain. The few available studies on the use of SNRIs in children looked at treatment of depression in adolescent patients. SNRIs have a greater benefit than SSRIs for neuropathic pain. Elevation of norepinephrine levels is thought to be necessary for an antidepressant to be effective against neuropathic pain, a property SNRIs share with TCAs but not with SSRIs.

Antiepileptic drugs

Antiepileptic drugs (AEDs), including valproic acid, carbamazepine, phenytoin, and lamotrigine, are used to treat adults with neuropathic and central pain. As they have more significant side effects than gabapentin or a TCA, and it is unclear whether they provide added benefit, they are considered third-line treatment for peripheral and central neuropathic pain in adults. One must be cautious when considering this class of medications for treating persistent pain behaviors in children who have SNI.

Cannabinoids

Cannabinoids may also have a role in pain management, though their use for children who have SNI has not been studied. Dronabinol is the synthetic form of delta-9-tetrahydrocannabinol (THC), an active compound of the cannabis plant (marijuana). Its mechanism of action includes an agonist effect at the cannabinoid (C_1 and C_2) receptors (Croxford 2003). Dronabinol is approved for use in chemotherapy-induced nausea and vomiting, as well as for anorexia secondary to acquired immunodeficiency syndrome (AIDS). It has also been studied in adult patients with CNS impairment, most notably MS and traumatic brain injury (Croxford 2003). Benefit for central pain and spasticity has been demonstrated in patients with MS (Collin et al. 2007; Rog et al. 2005; Svendsen, Jensen, and Bach 2004).

These findings provide theoretical reasons to consider cannabinoids for children with SNI who have refractory pain behaviors and associated symptoms such as spasticity. Side effects include delayed gastric emptying, an important consideration for children who have SNI. Other common side effects include dizziness, anxiety, depression, irritability, restlessness, tachycardia, and dry mouth.

Selecting the initial medication dose

The following information can be factored into selection of the initial dose of a medication:

- Response to prior medications
- Level of alertness: is it decreased from a prior baseline?
- Compromised breathing
- Use of other sedating medications

- Renal and liver functions
- Prioritizing the goal of reducing pain versus minimizing sedation

If the goal is to minimize sedation, the initial dose can be lowered from the suggested starting dose and then increased in a standardized manner until symptoms improve. This may delay the initiation of symptom relief. When sedation does occur, it is often transient once an effective dose has been determined. For moderate to severe symptoms, transient sedation is often considered acceptable, given the priority of improved symptom management. A patient receiving an unchanged dose of a medication can experience new-onset sedation in several ways: when a medication that can alter the metabolism of another, sedating medication is started or stopped; when the ability to clear a medication changes, as a result of decline in renal function; or when there is a reduction in pain stimulation.

Christina is a 2-year-old who has an anoxic injury to the CNS as a result of a cardiac arrest at 15 months of age. She is having episodes that include stiffening, arching, tachycardia with heart rates in the 190s, sweating, and facial flushing. She is described as being "miserable" on a daily basis. Her episodes have not improved despite treatment with tizanidine, baclofen, and lorazepam.

Gabapentin is started for Christina, because of its potential benefit for central neuropathic pain and autonomic dysfunction. Given the severity, frequency, and duration of her episodes, a dose of morphine sulfate is also given, with benefit noted within 30 minutes. Morphine is scheduled ATC, along with prn doses, to provide symptom relief as the gabapentin dose is increased every other day. Christina is more comfortable and awake by the next day, with a decrease in the severity and frequency of episodes.

Twenty-four hours after the third increase in the gabapentin dose, Christina is less alert, with a decrease in the amount of time she is awake. The scheduled morphine is withheld with prn remaining available, with two doses used in the following week. She is more awake and alert after scheduled morphine is stopped, yet remains more comfortable. This change in her level of alertness is thought to reflect a reduction in pain stimulation resulting from the gabapentin. Her comfort and tone remain significantly improved several months later.

Medication delivery: sublingual, intranasal, rectal, and skin patch

Some medications can be given in several different ways. Many that are taken orally or are given by G tube can also be given sublingually or

buccally. This is possible when the medication is readily absorbed through the mucous membranes. The medication is placed under the tongue (sublingual) or between the gum and the cheek (buccal).

The medications that can be taken sublingually or buccally are available as a concentrated liquid or as a small, quick-dissolving tablet. The option of sublingual/buccal can be of benefit for some children who have SNI and feeding tubes, such as when gastric emptying and intestinal motility slow down as the child's medical condition worsens. Some examples of medications are morphine and other opioids, including methadone; benzodiazepines such as midazolam and lorazepam; and hyoscyamine, as in treatment for secretions.

Intranasal delivery is another option for several medications (Wolfe and Braude 2010). These include fentanyl for intermittent pain management and midazolam for seizures, anxiety, and dyspnea.

Medications that can be given rectally include diazepam, clonazepam, and antiepileptic drugs, including phenobarbital, carbamazepine, lamotrigine, and valproic acid (Birnbaum et al. 2001; Epilepsy.com 2011; Smith, Sharkey, and Campbell 2001). Guidelines for rectal administration of drugs that are not in a prepackaged form (such as diazepam rectal [Diastat]) include how far to insert the catheter (i.e., the length) based on age (Smith, Sharkey, and Campbell 2001). Guidelines are provided in table 4.7. The total volume should be less than 60 to 80 mL for older children, with a smaller volume for children younger than 1 year (Smith, Sharkey, and Campbell 2001; Warren 1996).

Several skin patches are available for continuous delivery of some medications: fentanyl for chronic pain management; clonidine, such as for dysautonomia and as a pain adjuvant; and scopolamine, for nausea, vomiting, and secretion management. The fentanyl patch should *not* be used for acute

TABLE 4.7 Rectal delivery of medications

Age	Length to insert the catheter
1 month	1.5 cm
1 year	3.5 cm
2 years	4 cm
6 years	4.5 cm
10 years	6 cm

pain. The dose can be safely identified after determining the daily opioid dose needed for chronic pain control.

Summary of pain treatment

Management of discomfort includes comfort strategies such as repositioning, cuddling, rocking, massaging, warm baths, swaddling, and pleasurable activities such as music. For symptoms localized to the gut, strategies include venting of a G tube, equipment that allows venting during feeding (Farrell valve bag pressure relief system), and a decrease in the volume of fluids given by feeding tube. Integrative therapies, also referred to as complementary and alternative therapies, may be beneficial. Options include aromatherapy and acupuncture, though there is limited information about the role of such interventions for children who have SNI. Finally, equipment to consider includes seating systems and supportive pillows for positional pain, weighted blankets, and vibrating mats and pillows for vibratory stimulation.

Many children who have SNI and persistent pain behaviors benefit from a combination of these nonpharmacological interventions, along with a medication trial for the problems outlined in figure 4.1. The medications to consider for symptom management in children who have SNI are summarized in table 4.8.

Back to the case examples

Lars, the 3-year-old boy who has SNI as a result of CMV infection during pregnancy, is described as "90% back to his previous happy self" after initiation of gabapentin. Lars's symptoms remain resolved several years later.

Raymond has resolution of his symptoms and a significant improvement in sleep with gabapentin. His symptoms remain resolved 9 months later.

Dylan was being considered for Nissen fundoplication surgery. A palliative care consultation identifies increasing crying along with episodes of intermittent tachycardia, hypertension, sweating, and facial flushing.

Gabapentin and cyproheptadine are initiated. Dylan's autonomic features decrease significantly within several days. Irritability, crying, and arching improve by 25% to 50%. Nortriptyline is initiated 1 week later, with improvement in all symptoms within 5 days. He remains comfortable after reinitiation of G-tube feedings. The diazepam dose is titrated down without any changes

TABLE 4.8 Medications for empirical symptom treatment

Medications	Comments
Gabapentinoids: Thought to decrease stimulation (excitation) of nerves by binding to the alpha-2-delta subunit of voltage-dependent Ca^{2+} ion channels in the brain and spinal cord (CNS)	
Gabapentin (Neurontin) Pregabalin (Lyrica)	• Treatment of neuropathic pain, central pain, visceral hyperalgesia, dysautonomia, and spasticity • Both now available as a liquid • No significant interactions with other drugs • No evidence that one is superior to the other for children who have SNI
Tricyclic antidepressants (TCAs): Presynaptic reuptake inhibition of serotonin and norepinephrine in the CNS, both inhibitors of pain transmission	
Nortriptyline (Pamelor) Amitriptyline (Elavil)	• Treatment of neuropathic pain, central pain, and visceral hyperalgesia • Can be used in combination with gabapentin: one study identified greater benefit with the combination of gabapentin and nortriptyline for neuropathic pain in adults over either one given alone
Opioids: Opioid receptor agonists, including mu receptors	
Tramadol (Ultram) Morphine and other opioids Methadone	• Treatment of moderate to severe pain and autonomic storms • Tramadol may have added benefit as a result of its multiple receptor properties, though must be used cautiously in patients with a seizure disorder • Methadone may have benefit for neuropathic pain as an *N*-methyl-D-aspartate (NMDA) receptor antagonist, though requires expertise in use
Benzodiazepines: Increase affinity of gamma-aminobutyric acid (GABA) for $GABA_A$ receptors	
Diazepam (Valium) Lorazepam (Ativan) Midazolam (Versed) Clonazepam (Klonopin)	• Treatment of intermittent muscle spasms, mostly studied with diazepam though others may have similar benefit • Treatment of intermittent autonomic storms • Can result in tolerance with chronic, daily use • Can result in paradoxical effects such as increased agitation and irritability

TABLE 4.8 *(continued)*

Medications	Comments
	• Benzodiazepines must be tapered off very slowly after chronic use, typically a decrease every 7 days by an amount that is 5%–10% of the initial dose
Alpha-2 adrenergic receptor agonists	
Clonidine (Catapres) Tizanidine (Zanaflex)	• Treatment of spasticity and dysautonomia • May enhance pain treatment • Clonidine has advantage of availability as a liquid and transdermal patch • Tizanidine not well studied in children
Serotonin-2, histamine-1, and muscarinic (acetylcholine) receptor blocker	
Cyproheptadine (Periactin)	• Treatment of dysautonomia that includes associated retching and low body temperature (hypothermia)
Serotonin-norepinephrine reuptake inhibitors (SNRIs): Reuptake inhibition of serotonin and norepinephrine	
Venlafaxine (Effexor) Duloxetine (Cymbalta)	• Treatment of neuropathic pain: used as first- or second-line therapy in adults • Limited information on use in children • Not available as liquid • Cymbalta is an extended-release capsule that cannot be crushed
Cannabinoids: Cannabinoid receptor agonist (C_1 and C_2)	
Dronabinol (Marinol)	• Treatment of central pain in adults with multiple sclerosis: used as third-line therapy • Limited studies in children, including as an appetite stimulant in cancer patients

in symptoms. Because of greater improvement following initiation of nortriptyline, gabapentin is tapered, with an associated increase in irritability and crying. These behaviors improve after an increase back to the prior dose of gabapentin.

Grace's persistent irritability and disrupted sleep, with discomfort, remain significantly improved at 18 months after initiation of gabapentin.

At 4 years of age, Grace develops an escalation of pain symptoms following a respiratory illness. An exhaustive evaluation reveals nonspecific mild colitis. There is no improvement in pain symptoms following treatment of the colitis or with the use of intravenous (IV) opioids. Significant improvement is seen after nortriptyline is begun: Grace is described as "back to her old self." Given her improvement, gabapentin is later tapered with a goal to discontinue, resulting in an escalation of symptoms, which improve after resuming the original dose.

Methadone is later offered at a time of symptom escalation, with discussion recognizing the risk of prolonged QT. A review of goals identifies comfort management as the primary goal. A decision is made to initiate methadone, with steps taken to minimize risk, such as obtaining a nortriptyline level and being mindful of other medications that can alter the metabolism of methadone. There is also a decision not to obtain an ECG at baseline or following initiation of methadone, as the medication decisions will be based on the ability to improve comfort—the primary and overriding goal for decision making. Following initiation of methadone, improvement is noted. Grace remains on this combination of medications until her death, 9 months later, as a result of disease progression with respiratory failure.

Ellen's caregivers are asked whether they think pain may be a reason why she is more withdrawn. Though they initially are not sure, pain is identified as a potential source after they receive information about behaviors that can indicate pain in nonverbal individuals who have SNI. Features suggesting that Ellen is in pain include pursed lips, scrunching of her eyes, appearing "tense," and an "odd laugh." Evaluation for a pain source produces negative findings, including a gastric pH of 5 to 7 and guaiac-negative fecal test result, checked because Ellen is not taking an H-2 blocker or PPI.

Her antidepressant is stopped and a trial of gabapentin is initiated, starting at a smaller dose to minimize added sedation. Within the first week, Ellen appears more relaxed, more alert, and more interactive with her caregivers. The following week she is described as being "more than 50%" improved, including by one caregiver who was not aware of the medication trial. The benefit continues with further increases in her gabapentin dose to 300/300/600 mg daily, with half of the total dose given at night because of poor sleep.

PAIN BEHAVIORS THAT PERSIST DESPITE TREATING AN IDENTIFIED CAUSE

Based on anecdotal reports, an identified nociceptive source may not, in retrospect, be the source of pain and other symptoms. One example is

that of Tim, a 22-year-old who has cerebral palsy and SNI. He is noted to have persistent pain behaviors despite treatment of GERD and constipation. Further studies identify gallstones. Despite laparoscopic removal of the gallbladder, he continues to have pain behaviors weeks after surgery. Gabapentin is initiated, following the recommendation of a pediatric palliative care physician, with improvement in pain symptoms within one week. In retrospect, there was no gallbladder wall thickening and blood test results were normal, including liver enzymes and total bilirubin—increasing the possibility that the gallstones were an incidental finding and not the cause of symptoms. This again suggests the benefit of a symptom treatment trial before exploring all nociceptive causes of pain.

Four-year-old Grace provides another example, with the finding of nonspecific colitis on colonoscopy and no improvement in symptoms with anti-inflammatory treatment. In a similar case, an 8-year-old boy with SNI developed severe crying spells persisting for weeks at a time. Nonspecific colitis was identified on colonoscopy, with an escalation of symptoms following treatment with prednisone and sulfasalazine (Hauer, Wical, and Charnas 2007). Gabapentin resulted in a resolution of symptoms, but was later discontinued because of nystagmus. Symptoms again resolved after initiation of amitriptyline.

Though these cases are anecdotal, and one must be cautious with specific interpretation, they highlight the importance of considering empirical symptom treatment trials early in the process of searching for the source of pain behaviors. These examples also raise the question, are children who have SNI at risk for certain incidental findings (findings that are not causing symptoms)? One might consider, though there is no evidence, the potential risk for gallstones and sludge associated with tube feedings and the potential for nonspecific colitis in children with chronic constipation.

HOPING AND PREPARING: MY CHILD'S SYMPTOMS ARE BETTER, BUT I WISH WE WERE SEEING MORE IMPROVEMENT

Most children with SNI who have distressing symptoms can be expected, with treatment, to have reduced pain and other symptoms, though not all will have the improvement hoped for. Most will have some improvement, many will have significant improvement, some will have improvement that is less than desired, and some will have a return of symptoms. Knowing about the range of outcomes can help parents prepare. There is a need

to balance, on the one hand, the search for an explanation and a better treatment option and, on the other hand, the consideration that the problem and associated symptoms may be intractable. Pain behaviors, increasing muscle tone with posturing and arching, and persistent feeding intolerance with retching and vomiting are examples of potentially intractable problems, explored in greater detail in chapters 5 and 7.

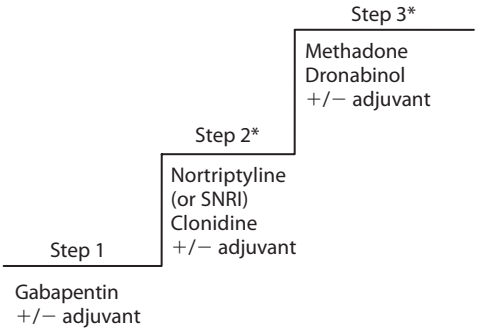
SUMMARY

When concerns about pain arise for a child who has SNI, an evaluation for a nociceptive source of pain should be initiated. When pain behaviors persist despite treatment of an identified source, or when pain appears to be out of proportion to the source, or when no source is found, some children benefit from an empirical trial of gabapentin. If there is partial improvement, nortriptyline or clonidine can be added and used in combination with gabapentin.

Treatment should be considered for other sources of pain behaviors or associated problems, such as clonidine for autonomic dysfunction or cyproheptadine for retching. In addition, as-needed medications can be used for intermittent problems, such as clonidine, a benzodiazepine, or an opioid for intermittent muscle spasms, autonomic storms, or breakthrough pain. When pain behaviors continue despite these steps, methadone is a third-line option, but it requires expertise in use. In addition, there are theoretical reasons to consider dronabinol and serotonin-norepinephrine reuptake inhibitors, though these must be used cautiously. With limited evidence to guide us, we must be careful about introducing too many medication trials.

Figure 4.4 and table 4.9 provide suggested step-by-step guidelines for evaluation and management of neurologically impaired children with behaviors indicating pain. Ultimately, an improved awareness of all potential sources of discomfort and distress in children who have SNI will expand our ability to improve comfort in this vulnerable group of children.

George is a 27-year-old who has a history of birth asphyxia, with associated spastic quadriplegia, seizure disorder, cortical blindness, and G-tube placement. His history is significant for recurrent episodes of pain behaviors, noted as crying, facial grimacing, stiffening, arching, and inconsolability. Episodes are cyclical, with multiple daily episodes occurring for 7 to 10 days each month, then less frequently in other weeks. Pain episodes are typically rated 7 to 10 on the INRS pain scale. Interventions during pain episodes have variable



- "Neuro-pain": used to indicate children with SNI and persistent pain behaviors
- *Steps 2 and 3: pain unrelieved by medication in previous step
- Adjuvant (enhances benefit of other treatment):
  - — Breakthrough pain: prn acetaminophen, ibuprofen, tramadol, or opioid
  - — Autonomic storms: prn clonidine, opioid, or benzodiazepine
  - — Muscle spasms: prn clonidine or benzodiazepine
  - — Retching: cyproheptadine
  - — Autonomic dysfunction: propranolol or metoprolol

Figure 4.4. Neuro-pain ladder

benefit, including repositioning, G-tube venting, acetaminophen, ibuprofen, oxybutynin, Maalox, and morphine sulfate. Replacing G-tube feedings with Pedialyte gives some benefit, but is limited to 24 hours at a time so as not to restrict nutrition. Potential sources of pain include urinary retention, recurrent UTI, and nonobstructive renal calculi. His history is also significant for constipation, intestinal dysmotility, pseudo-obstruction, and hypertension.

Prior interventions without benefit have included erythromycin for intestinal motility, Farrell bag for venting of the G tube, empirical treatment for *H. pylori*, and an empirical trial of sucralfate. Chronic treatment of potential pain sources includes management of constipation and treatment of GERD with an H-2 blocker and PPI. Treatment of other problems includes baclofen, 20 mg four times daily, for spasticity and carbamazepine for seizures, with no seizure for more than 1 year. George's hypertension is treated with clonidine three times per day (TID) and amlodipine daily. Recent evaluation remains unremarkable, including dental examination (routine), ophthalmology examination (negative for glaucoma), hip and spine X-rays (stable), renal stones (stable, with no obstruction on repeat abdominal CT [computed tomograph] scans), and multiple recent urine analyses (negative for white cells and blood).

Earlier treatment has included amitriptyline, initiated by a gastroenterologist 1 year ago, then discontinued several weeks later following an increase in seizures. Of note, the dose was started at 0.5 mg/kg rather than 0.2 mg/kg (maximum starting dose 10 mg), which may have contributed to the side effects.

TABLE 4.9 Step-by-step suggestions for pain management

1. Identify the presence of behaviors associated with pain (chapter 3).
2. Evaluate for potential causes (figures 4.1 and 4.2, table 4.1).
3. Assess the severity of pain as well as the frequency and duration of episodes.
4. Treat identified causes when possible and if consistent with goals of care.
5. Maximize the management of chronic problems such as constipation and GERD.
6. Initiate *gabapentin trial*—reasons to consider include the following:
   - No nociceptive pain source identified
   - Symptoms persist despite treating identified source(s)
   - Symptoms include sudden bursts of intense, recurrent pain behaviors
   - Onset of symptoms occurs weeks to months following surgery
   - Painful peripheral neuropathy associated with disease
   - Symptoms suggest central neuropathic pain/visceral hyperalgesia, such as pain associated with tube feedings, intestinal gas, and bowel movements
   - Symptoms include muscle spasms and autonomic dysfunction
7. Utilize *as-needed medications for muscle spasms, autonomic storms, and breakthrough pain*, such as clonidine, morphine, or a benzodiazepine (figure 4.4).
8. Review prior experience with sedating medications to guide initial dosage selection.
9. Assess for improvement, which can include a pain assessment tool (quantitative data are beneficial, but it is helpful not to become overly dependent on numbers).
   - Have the pain behaviors improved?
   - Have the severity, frequency, and duration of the episodes decreased?
   - How much improvement in severity or decrease in frequency and duration of pain do you estimate: is your child 25% improved, 50% improved, more than 50% improved?
10. *If partial but not adequate improvement in symptoms, continue gabapentin and consider adding the following:*
    - *Tricyclic antidepressant (nortriptyline or amitriptyline)* for pain-predominant features, including symptoms localized to the GI tract
    - *Clonidine* for autonomic dysfunction–predominant features and/or intermittent muscle spasms
    - *Cyproheptadine* for associated retching
11. Consider *methadone* for pain behaviors that persist despite the above steps (requires expertise in use).
    - Dose adjustments should not occur more often than every 72 hours, given its biphasic elimination.
    - Other medications can alter the metabolism of methadone, resulting in a change in its blood level.

TABLE 4.9 *(continued)*

12. *Benzodiazepines* are best used intermittently (autonomic storms, muscle spasms) or as a short-term bridge.
13. Identify a timeline within which an intervention is expected to provide improvement, factoring in when the peak effect is expected, the need to titrate medication, and the frequency of symptoms.
14. If there is suboptimal benefit within the time interval identified, determine whether the intervention will be continued or discontinued before initiating other interventions.
15. If an intervention is discontinued, determine whether it requires tapering before stopping. In general, baclofen, clonidine, and gabapentin can be tapered off over 2 to 4 weeks, such as decreasing by 10% to 20% of the initial dose every 2 to 3 days; tapering of benzodiazepines and opioids depends on the duration of use; chronic use of benzodiazepines, opioids, TCAs, and SNRIs requires longer tapering schedules, often over 4 to 12 weeks or longer, such as decreasing by 10% of the initial dose every 7 days.

Gabapentin was then started, remaining at 200 mg TID for the past year, more recently increased to 600 mg TID, with good days described as "great" and with improved sleep. Unfortunately, George continued to have pain episodes with only mild improvement.

The morphine sulfate dose was increased by 50% on two separate occasions, with no benefit. Autonomic dysfunction with autonomic storms was considered, given his history of hypertension, bowel dysmotility, and episode of pseudo-obstruction. In addition to scheduled clonidine, prn clonidine was used as often as every 4 hours for pain episodes, with variable benefit.

An empirical trial with venlafaxine was initiated, given the ongoing frequency and severity of pain episodes without a source. This medication was selected because of the increase in seizures when George was taking a TCA. Prior to this trial, the results of a repeat urine analysis were normal and abdominal CT scan was unchanged. Since starting venlafaxine, George has been pain free for 6 months, with the exception of symptoms at the time of a UTI. He has required no prn medications, with the exception of acetaminophen for fever with mild discomfort, with his urine analysis significant for 20 to 50 WBCs (white blood cells per high-power field); this was treated with an antibiotic, with resolution of symptoms. In addition, his spasticity has improved, and vomiting has decreased from an average of four times per week to an episode every 1 to 3 weeks. The goal is to monitor for continued benefit for 12 months and then consider a gradual taper of gabapentin to determine whether there is a continued need for symptom management.

Key points from this case history:

- Central neuropathic pain / visceral hyperalgesia should be considered when frequent pain episodes occur in the setting of known nociceptive pain sources in the gut.
- Improvement with "gut rest," by replacing tube feedings with an electrolyte solution for hydration, may be an indirect indicator of central pain / visceral hyperalgesia as a pain source.
- Pain episodes in individuals who have SNI may not respond to morphine sulfate.
- Pain management benefits from a stepwise approach, with consideration of different pain sources and medications with different mechanisms of action. Some patients may eventually receive significant benefit after three or four empirical trials.
- Pain treatment will not mask symptoms from a new pain source, though it may lessen the severity of symptoms if hyperalgesia was contributing to the severity of pain.

TAKE-HOME POINTS

- Pain is a frequent problem in children who have SNI.
- Pain frequency and intensity are higher in those with greater neurological impairment.
- A systematic approach can shorten the time required to improve a child's comfort.
- Sources of nociceptive pain (tissue injury and inflammation) are summarized in table 4.1.
- Neuropathic pain, central pain, and visceral hyperalgesia should be considered in the following circumstances:
  - Symptoms persist despite treating nociceptive (tissue injury) sources of pain.
  - No nociceptive source is identified.
  - Symptoms include brief bursts of intense, recurrent pain behaviors.
  - Symptoms suggest visceral hyperalgesia and the visceral symptoms associated with central pain (pain associated with tube feedings, intestinal gas, and bowel movements).
  - Symptoms are noted weeks or months following surgery.
  - Symptoms include muscle spasms and features associated with dysautonomia.

- Medication toxicity and withdrawal can result in the same features as behaviors associated with pain.
- Gabapentin is a safe first-line trial medication when neuropathic pain, central pain, and/or visceral hyperalgesia are suspected.
- Nortriptyline is suggested as a second-line trial medication and can be used along with gabapentin when symptoms are partially responsive to gabapentin.
- Clonidine, as an alternative, may be beneficial when autonomic dysfunction or muscle spasms are the predominant features associated with pain behaviors.
- Cyproheptadine may be helpful when associated symptoms include retching and vomiting.
- Intermittent muscle spasms may be reduced by as-needed benzodiazepine or clonidine, and intermittent autonomic storms by as-needed morphine, clonidine, or benzodiazepine.
- Nociceptive pain sources and neuropathic pain can coexist. This can be suggested by pain behaviors that appear to be out of proportion to the identified cause, such as prolonged and excessive crying in a child with GERD, or symptoms that are not eliminated after an identified source has been treated.
- Nonpharmacological interventions are always an essential part of symptom management.
- Other sources of distress and discomfort include retching, vomiting, muscle spasms, dystonia, excessive respiratory secretions, and dyspnea. Medical care and symptom plans are reviewed in chapters 5, 6, and 7.

References

Axelrod FB, Berlin D. 2009. Pregabalin: a new approach to treatment of the dysautonomic crisis. *Pediatrics* 124(2):743–46.

Baguley IJ. 2008. Autonomic complications following central nervous system injury. *Semin Neurol* 28(5):716–25.

Baguley IJ, Cameron ID, Green AM, et al. 2004. Pharmacological management of dysautonomia following traumatic brain injury. *Brain Inj* 18(5):409–17.

Baguley IJ, Heriseanu RE, Gurka JA, et al. 2007. Gabapentin in the management of dysautonomia following severe traumatic brain injury: a case series. *J Neurol Neurosurg Psychiatry* 78(5):539–41.

Berde CB, Lebel AA, Olsson G. 2003. Neuropathic pain in children. In *Pain in Infants, Children, and Adolescents*, ed. Schechter NL, Berde CB, Yaster M, pp. 620–41. Philadelphia: Lippincott Williams and Wilkins.

Bernard SA, Bruera E. 2000. Drug interactions in palliative care. *J Clin Oncol* 18(8): 1780–99.

Birnbaum AK, Kriel RL, Im Y, Remmel RP. 2001. Relative bioavailability of lamotrigine chewable dispersible tablets administered rectally. *Pharmacotherapy* 21(2):158–62.

Boyer EW, Shannon M. 2005. The serotonin syndrome. *N Engl J Med* 352(11):1112–20.

Breau LM, Camfield C, McGrath PJ, et al. 2001. Measuring pain accurately in children with cognitive impairments: refinement of a caregiver scale. *J Pediatr* 138(5):721–27.

Breau LM, Camfield CS, McGrath PJ, Finley GA. 2003. The incidence of pain in children with severe cognitive impairments. *Arch Pediatr Adolesc Med* 157(12):1219–26.

Breau LM, Camfield CS, McGrath PJ, Finley GA. 2004. Risk factors for pain in children with severe cognitive impairments. *Dev Med Child Neurol* 46(6):364–71.

Browne TR. 1976. Clonazepam: a review of a new anticonvulsant drug. *Arch Neurol* 33(5): 326–32.

Browne TR. 1978. Clonazepam. *N Engl J Med* 299(15):812–16.

Bruera E, Sweeney C. 2002. Methadone use in cancer patients with pain: a review. *J Palliat Med* 5(1):127–38.

Canavero S, Bonicalzi V. 2007. *Central Pain Syndrome: Pathophysiology, Diagnosis, and Management*. New York: Cambridge University Press.

Carter B, McArthur E, Cunliffe M. 2002. Dealing with uncertainty: parental assessment of pain in their children with profound special needs. *J Adv Nurs* 38(5):449–57.

Chelimsky G, Chelimsky T. 2001. Familial association of autonomic and gastrointestinal symptoms. *Clin Auton Res* 11(6):383–86.

Chelimsky G, Hupertz VF, Chelimsky TC. 1999. Abdominal pain as the presenting symptom of autonomic dysfunction in a child. *Clin Pediatr (Phila)* 38(12):725–29.

Ciszkowski C, Madadi P, Phillips MS, et al. 2009. Codeine, ultrarapid-metabolism genotype, and postoperative death. *N Engl J Med* 361(8):827–28.

Collin C, Davies P, Mutiboko IK, Ratcliffe S, Sativex Spasticity in MS Study Group. 2007. Randomized controlled trial of cannabis-based medicine in spasticity caused by multiple sclerosis. *Eur J Neurol* 14(3):290–96.

Complex Child E-Magazine. 2009. Neuro-crying, neuro-irritability, or pain? A personal account. www.articles.complexchild.com/nov2009/00166.html.

Complex Child E-Magazine. 2009. Vibration for pain control and calming. www.articles.complexchild.com/sept2009/00152.html.

Croxford JL. 2003. Therapeutic potential of cannabinoids in CNS disease. *CNS Drugs* 17(3): 179–202.

Cutter N, Scott DD, Johnson JC, Whiteneck G. 2000. Gabapentin effect on spasticity in multiple sclerosis: a placebo-controlled, randomized trial. *Arch Phys Med Rehabil* 81(2):164–69.

Dean M. 2004. Opioids in renal failure and dialysis patients. *J Pain Symptom Manage* 28(5): 497–504.

Delgado MR, Hirtz D, Alsen M, et al. 2010. Practice parameter: pharmacologic treatment of spasticity in children and adolescents with cerebral palsy (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. *Neurology* 74(4):336–43.

Delgado-Aros S, Camilleri M. 2005. Visceral hypersensitivity. *J Clin Gastroenterol* 39(Suppl 3): S194–203.

Devlin JW, Roberts RJ. 2009. Pharmacology of commonly used analgesics and sedatives in the ICU: benzodiazepines, propofol, and opioids. *Crit Care Clin* 25(3):431–49.

Diesing TS, Wijdicks EF. 2006. Arc de cercle and dysautonomia from anoxic injury. *Mov Disord* 21(6):868–69.

Ducharme C, Carnevale FA, Clermont MS, Shea S. 2005. A prospective study of adverse reactions to the weaning of opioids and benzodiazepines among critically ill children. *Intensive Crit Care Nurs* 21(3):179–86.

Dworkin RH, O'Connor AB, Backonja M, et al. 2007. Pharmacologic management of neuropathic pain: evidence-based recommendations. *Pain* 132:237–51.

Epilepsy.com. 2011. Antiepileptic drugs (AEDs) available for rectal administration. http://professionals.epilepsy.com/page/table_procedures_rectal.html.

Finnerup NB, Otto M, McQuay HJ, et al. 2005. Algorithm for neuropathic pain treatment: an evidence based proposal. *Pain* 118(3):289–305.

Fisher D. 2010. Opioid tapering in children: a review of the literature. *AACN Adv Crit Care* 21(2):139–45.

Franck LS, Naughton I, Winter I. 2004. Opioid and benzodiazepine withdrawal symptoms in paediatric intensive care patients. *Intensive Crit Care Nurs* 20(6):344–51.

Frese A, Husstedt IW, Ringelstein EB, Evers S. 2006. Pharmacologic treatment of central post-stroke pain. *Clin J Pain* 22(3):252–60.

Gan TJ. 2006. Pharmacokinetic and pharmacodynamic characteristics of medications used for moderate sedation. *Clin Pharmacokinet* 45(9):855–69.

Gardner JS, Blough D, Drinkard CR, et al. 2000. Tramadol and seizures: a surveillance study in a managed care population. *Pharmacotherapy* 20(12):1423–31.

Gilron I, Bailey JM, Tu D, et al. 2009. Nortriptyline and gabapentin, alone and in combination for neuropathic pain: a double-blind, randomised controlled crossover trial. *Lancet* 374(9697):1252–61.

Greco C, Berde CB. 2005. Pain management for the hospitalized pediatric patient. *Pediatr Clin N Am* 52:995–1027.

Haig GM, Bockbrader HN, Wesche DL, et al. 2001. Single-dose gabapentin pharmacokinetics and safety in healthy infants and children. *J Clin Pharmacol* 41(5):507–14.

Hasler ML. 2003. Pharmacotherapy for intestinal motor and sensory disorders. *Gastroenterol Clin North Am* 32(2):707–32.

Hauer J, Wical B, Charnas L. 2007. Gabapentin successfully manages chronic unexplained irritability in children with severe neurologic impairment. *Pediatrics* 119(2):e519–22.

Hibbs AM, Lorch SA. 2006. Metoclopramide for the treatment of gastroesophageal reflux disease in infants: a systematic review. *Pediatrics* 118(2):746–52.

Houghton LA, Fell C, Whorwell PJ, et al. 2007. Effect of a second-generation alpha2delta ligand (pregabalin) on visceral sensation in hypersensitive patients with irritable bowel syndrome. *Gut* 56(9):1218–25.

Houlihan CM, O'Donnell M, Conaway M, Stevenson RD. 2004. Bodily pain and health-related quality of life in children with cerebral palsy. *Dev Med Child Neurol* 46: 305–10.

Hugel H, Ellershaw JE, Dickman A. 2003. Clonazepam as an adjuvant analgesic in patients with cancer-related neuropathic pain. *J Pain Symptom Manage* 26(6):1073–74.

Hunt A, Goldman A, Seers K, et al. 2004. Clinical validation of the paediatric pain profile. *Dev Med Child Neurol* 46(1):9–18.

Hunt A, Mastroyannopoulou K, Goldman A, Seers K. 2003. Not knowing—the problem of pain in children with severe neurological impairment. *Int J Nurs Stud* 40(2):171–83.

Hunt A, Wisbeach A, Seers K, et al. 2007. Development of the paediatric pain profile: role of video analysis and saliva cortisol in validating a tool to assess pain in children with severe neurological disability. *J Pain Symptom Manage* 33(3):276–89.

IASP (International Association for the Study of Pain). 2011. IASP taxonomy pain terms. www.iasp-pain.org/Content/NavigationMenu/GeneralResourceLinks/PainDefinitions/default.htm.

Jackson N, Doherty J, Coulter S. 2008. Neuropsychiatric complications of commonly used palliative care drugs. *Postgrad Med J* 84(989):121–26.

Kalachnik JE, Hanzel TE, Sevenich R, Harder SR. 2002. Benzodiazepine behavioral side effects: review and implications for individuals with mental retardation. *Am J Ment Retard* 107(5):376–410.

Kalachnik JE, Hanzel TE, Sevenich R, Harder SR. 2003. Brief report: clonazepam behavioral side effects with an individual with mental retardation. *J Autism Dev Disord* 33(3):349–54.

Kehlet H, Jensen TS, Woolf CJ. 2006. Persistent postsurgical pain: risk factors and prevention. *Lancet* 367:1618–25.

Klit H, Finnerup NB, Jensen TS. 2009. Central post-stroke pain: clinical characteristics, pathophysiology, and management. *Lancet Neurol* 8(9):857–68.

Kloos RT. 1995. Spontaneous periodic hypothermia. *Medicine (Baltimore)* 74(5):268–80.

Kong CK, Wong HS. 2005. Weight-for-height values and limb anthropometric composition of tube-fed children with quadriplegic cerebral palsy. *Pediatrics* 116(6):e839–45.

Korn-Merker E, Borusiak P, Boenigk HE. 2000. Gabapentin in childhood epilepsy: a prospective evaluation of efficacy and safety. *Epilepsy Res* 38(1):27–32.

Kuiken SD, Tytgat GN, Boeckxstaens GE. 2005. Review article: drugs interfering with visceral sensitivity for the treatment of functional gastrointestinal disorders—the clinical evidence. *Aliment Pharmacol Ther* 21(6):633–51.

Kuperminc MN, Gurka MJ, Bennis JA, et al. 2010. Anthropometric measures: poor predictors of body fat in children with moderate to severe cerebral palsy. *Dev Med Child Neurol* 52(9):824–30.

Lader M, Tylee A, Donoghue J. 2009. Withdrawing benzodiazepines in primary care. *CNS Drugs* 23(1):19–34.

Lauder GR, White MC. 2005. Neuropathic pain following multilevel surgery in children with cerebral palsy: a case series and review. *Paediatr Anaesth* 15(5):412–20.

Lee KJ, Kim JH, Cho SW. 2005. Gabapentin reduces rectal mechanosensitivity and increases rectal compliance in patients with diarrhoea-predominant irritable bowel syndrome. *Aliment Pharmacol Ther* 22(10):981–88.

Liptak GS. 2005. Complementary and alternative therapies for cerebral palsy. *Ment Retard Dev Disabil Res Rev* 11(2):156–63.

Lundeberg T. 1984. Long-term results of vibratory stimulation as a pain relieving measure for chronic pain. *Pain* 20(1):13–23.

Lundeberg T, Abrahamsson P, Bondesson L, Haker E. 1987. Vibratory stimulation compared to placebo in alleviation of pain. *Scand J Rehabil Med* 19(4):153–58.

Lundy CT, Doherty GM, Fairhurst CB. 2009. Botulinum toxin type A injections can be an effective treatment for pain in children with hip spasms and cerebral palsy. *Dev Med Child Neurol* 51(9):705–10.

Miller LG, Jankovic J. 1989. Metoclopramide-induced movement disorders: clinical findings with a review of the literature. *Arch Intern Med* 149(11):2486–92.

Moulin DE, Clark AJ, Gilron I. 2007. Pharmacological management of chronic neuropathic pain: consensus statement and guidelines from the Canadian Pain Society. *Pain Res Manag* 12(1):13–21.

Moulin DE, Palma D, Watling C, Schulz V. 2005. Methadone in the management of intractable neuropathic noncancer pain. *Can J Neurol Sci* 32(3):340–43.

Mousa H, Caniano DA, Alhajj M, et al. 2006. Effect of Nissen fundoplication on gastric motor and sensory functions. *J Pediatr Gastroenterol Nutr* 43(2):185–89.

Murphy EJ. 2005. Acute pain management pharmacology for the patient with concurrent renal or hepatic disease. *Anaesth Intensive Care* 33(3):311–22.

Nicholson BD. 2004. Evaluation and treatment of central pain syndromes. *Neurology* 62(5 Suppl 2):S30–36.

Park ES, Park CI, Cho SR, et al. 2002. Assessment of autonomic nervous system with analysis of heart rate variability in children with spastic cerebral palsy. *Yonsei Med J* 43(1):65–72.

Perquin CW, Hazebroek-Kampschreur AA, Hunfeld JA, et al. 2000. Pain in children and adolescents: a common experience. *Pain* 87(1):51–58.

Riss J, Cloyd J, Gates J, Collins S. 2008. Benzodiazepines in epilepsy: pharmacology and pharmacokinetics. *Acta Neurol Scand* 118(2):69–86.

Rivard PF, Nugent AC, Symons FJ. 2009. Parent-proxy ratings of pain before and after botulinum toxin type A treatment for children with spasticity and cerebral palsy. *Clin J Pain* 25:413–17.

Rog DJ, Nurmikko TJ, Friede T, Young CA. 2005. Randomized, controlled trial of cannabis-based medicine in central pain in multiple sclerosis. *Neurology* 65(6):812–19.

Ruiz C, Gener B, Garaizar C, Prats JM. 2003. Episodic spontaneous hypothermia: a periodic childhood syndrome. *Pediatr Neurol* 28(4):304–6.

Semenchuk MR, Sherman S. 2000. Effectiveness of tizanidine in neuropathic pain: an open-label study. *J Pain* 1(4):285–92.

Shelton RC. 2001. Steps following attainment of remission: discontinuation of antidepressant therapy. *Prim Care Companion J Clin Psychiatry* 3(4):168–74.

Sheth RD, Barron TF, Hartlage PL. 1994. Episodic spontaneous hypothermia with hyperhidrosis: implications for pathogenesis. *Pediatr Neurol* 10(1):58–60.

Smith H, Elliott J. 2001. Alpha2 receptors and agonists in pain management. *Curr Opin Anaesthesiol* 14:513–18.

Smith S, Sharkey I, Campbell D. 2001. Guidelines for rectal administration of anticonvulsant medication in children. *Paediatr Perinat Drug Ther* 4(4):140–47.

Stallard P, Williams L, Velleman R, et al. 2002. Brief report: behaviors identified by caregivers to detect pain in noncommunicating children. *J Pediatr Psychol* 27(2):209–14.

Strouse TB. 2009. Pharmacokinetic drug interactions in palliative care: focus on opioids. *J Palliat Med* 12(11):1043–50.

Svedberg LE, Englund E, Malker H, Stener-Victorin E. 2008. Parental perception of cold extremities and other accompanying symptoms in children with cerebral palsy. *Eur J Paediatr Neurol* 12(2):89–96.

Svendsen KB, Jensen TS, Bach FW. 2004. Does the cannabinoid dronabinol reduce central pain in multiple sclerosis? Randomised double blind placebo controlled crossover trial. *BMJ* 329(7460):253.

Taddio A, Oberlander TF. 2006. Pharmacological management of pain in children and youth with significant neurological impairments. In *Pain in Children and Adults with Developmental Disabilities*, ed. Oberlander TF, Symons FJ, pp. 193–211. Baltimore: Brookes Publishing.

Tanaka E. 1999. Clinically significant pharmacokinetic drug interactions with benzodiazepines. *J Clin Pharm Ther* 24(5):347–55.

Temel JS, Greer JA, Muzikansky A, et al. 2010. Early palliative care for patients with metastatic non-small-cell lung cancer. *N Engl J Med* 363(8):733–42.

van Maldegem BT, Smit LM, Touw DJ, Gemke RJ. 2002 Neuroleptic malignant syndrome in a 4-year-old girl associated with alimemazine. *Eur J Pediatr* 161(5):259–61.

Warren DE. 1996. Practical use of rectal medications in palliative care. *J Pain Symptom Manage* 11(6):378–87.

Williams DG, Patel A, Howard RF. 2002. Pharmacogenetics of codeine metabolism in an urban population of children and its implications for analgesic reliability. *Br J Anaesth* 89(6):839–45.

Wolfe TR, Braude DA. 2010. Intranasal medication delivery for children: a brief review and update. *Pediatrics* 126(3):532–37.

Zangen T, Ciarla C, Zangen S, et al. 2003. Gastrointestinal motility and sensory abnormalities may contribute to food refusal in medically fragile toddlers. *J Pediatr Gastroenterol Nutr* 37(3):287–93.

CHAPTER 5

Gastrointestinal Problems
Retching, Vomiting, Feeding Intolerance, and Other Problems

Trust your instinct to the end, though you can render no reason.
—Ralph Waldo Emerson

Children who have severe neurological impairment encounter a number of problems related to the gastrointestinal tract and other organs in the abdomen. These problems can be both distressing for the child and challenging for parents and healthcare providers to manage. This chapter covers the common problems of retching, vomiting, gastroesophageal reflux, constipation, impaired intestinal motility, and feeding intolerance. Acute pancreatitis, gallstones, small bowel bacterial overgrowth, bladder dysfunction, urinary tract infection, and renal stones are also reviewed.

RETCHING AND VOMITING

Retching and vomiting are common in children who have SNI. There are several causes to consider. Some problems are the primary cause of vomiting; some, such as constipation, contribute; and others, such as dysautonomia, are a result of the impaired nervous system. To start, it is helpful to distinguish some of the terms commonly used:

- *Nausea* is a feeling of sickness in the stomach, characterized by an urge to vomit.
- *Vomiting* is the forceful ejection of stomach contents through the mouth as a result of spasmodic, involuntary contractions of the intestinal tract, abdomen, and diaphragm.

- *Retching* (gagging, dry heaves), involving the same mechanisms as vomiting but without ejection of stomach contents, is considered the first phase of the vomiting reflex.
- *Regurgitation* is the effortless return of small amounts of food or secretions to the mouth.

Symptoms associated with both vomiting and retching include sweating, increased heart rate, and appearing pale and in distress. These symptoms are not seen with regurgitation. Understanding these distinctions helps to guide consideration of the causes of vomiting and thus management decisions. Often, management is empirical, guided by details in a child's history. Initiating a medication trial can help avoid unnecessary testing for many children.

Keeping these definitions and this information in mind, we can break down the causes of vomiting into the mechanisms that trigger vomiting, known as the *vomiting reflex*, and the specific problems that cause vomiting. When vomiting first occurs, causes to consider include acute infectious gastroenteritis, acute pancreatitis, urinary tract infection (UTI), nephrolithiasis (kidney stones), gallstones with gallbladder inflammation or infection, and mechanical obstruction of the bowel, such as from adhesions or superior mesenteric artery syndrome (SMAS).

This chapter focuses on causes of persistent vomiting. Children who have SNI have an increased risk for retching and vomiting that become chronic, which can occur when input from the central nervous system to the enteric nervous system in the gut is altered. The enteric nervous system is a network of nerves in the gut, which is partly controlled by the CNS through the autonomic nervous system.

Table 5.1 reviews the causes of recurrent retching and vomiting in children who have SNI. As with pain, the goal is to identify and treat causes when possible, as well as to consider medications that can provide symptom relief. For example, medications may be used to block stimulation of the vomiting reflex. The mechanisms that trigger the vomiting reflex involve a complex array of receptors that, when stimulated, trigger retching and vomiting. Antiemetic medications block these receptors.

Gastroesophageal reflux disease

Gastroesophageal reflux (GER) is an important place to start, because it affects many children who have SNI. GER is the effortless movement of gastric content across the lower esophageal sphincter (LES) into the

TABLE 5.1 Acute and chronic causes of retching and vomiting

Cause	Treatment	Comments
Acute causes of new-onset vomiting	• Assess for possible causes: history of vomiting with diarrhea to suggest gastroenteritis; lab tests such as urine analysis and culture, amylase, lipase, ALT, t bili, alk phos; X-ray studies if concern for obstruction, such as upper gastrointestinal series (UGI) or abdominal CT scan • Treat the identified cause	Causes to consider include stomach flu (acute gastroenteritis), inflammation of the pancreas (pancreatitis), bladder infection (UTI), kidney stones, gallstones with gallbladder inflammation; mechanical obstruction such as from twisting of the bowels (volvulus), superior mesenteric artery syndrome (risk factors include sudden weight loss or following spinal surgery), or adhesions (fibrous bands that can form between tissue and organs following abdominal surgery)
Gastroesophageal reflux disease, motility disorders	• H-2 blockers and PPIs • Protective barrier: sucralfate • Promotility drugs: erythromycin, metoclopramide • Jejunostomy feeding tube	Motility disorders can be a result of impaired input from the brain to the nervous system of the gut (enteric nervous system); suggested by bloating, distension, retching, vomiting, discomfort; other problems can contribute, including constipation
Vomiting reflex	• Medications that block the 5HT-2, 5HT-3, H-1, Ach, and D-2 receptors	Suggested by retching, forceful vomiting, and associated symptoms such as sweating, pale skin, and the appearance of distress
Visceral hyperalgesia	• Gabapentin • Tricyclic antidepressants	Suggested by pain, retching, and vomiting associated with gastric feedings, intestinal feedings, intestinal gas, flatus, and bowel movements
Autonomic dysfunction	• Gabapentin • Clonidine • Cyproheptadine (symptoms of retching and hypothermia)	Suggested by retching and vomiting associated with sweating, redness or pallor of skin, increased saliva/secretions, agitation, distress, arching

(continued)

TABLE 5.1 *(continued)*

Cause	Treatment	Comments
Pseudo-obstruction	• Conservative management • Erythromycin • Neostigmine and pyridostigmine	Suggested by recurrent episodes of abdominal distension, pain, vomiting, and severe constipation, in the absence of mechanical obstruction
Constipation	• Polyethylene glycol • Lactulose • Senna • Bisacodyl suppository	Constipation will worsen and contribute to all sources of retching and vomiting; in addition, it is a stimulus of visceral hyperalgesia through distension of the colon

Abbreviations: Ach, acetylcholine; alk phos, alkaline phosphatase; ALT, alanine aminotransferase; D, dopamine; H, histamine; 5HT, serotonin; PPI, proton pump inhibitor; t bili, total bilirubin.

esophagus. GER is called gastroesophageal reflux disease (GERD) when this process occurs chronically, leading to symptoms, tissue inflammation, and injury. GER is not associated with forceful contraction of the abdominal wall, as happens when the vomiting reflex is stimulated. However, untreated GERD and excessive gastric acid can cause esophagitis and gastritis, which in turn can lead to stimulation of the vomiting reflex via vagus nerve input from the GI tract into the vomiting center.

GERD is an important cause to diagnose and treat early in a child with SNI who has vomiting and pain. It is equally important to consider the other causes of pain and vomiting when symptoms persist despite treatment for GERD. In addition to irritability and persistent vomiting, other problems that may suggest GERD include aversion to oral feeding, respiratory symptoms such as wheezing and congestion, hematemesis (blood in the material vomited), iron-deficiency anemia, and irritability with arching, referred to as Sandifer syndrome (Del Giudice et al. 1999; de Veer et al. 2008; Sherman et al. 2009). It is also important to consider other reasons for arching and irritability in children who have SNI, such as dystonic reactions in response to dopamine antagonists (metoclopramide, risperidone), hypertonia, and pain from other causes, as discussed in chapter 7.

Evaluation of GERD involves clinical suspicion and decisions on diagnostic tests. Studies include upper gastrointestinal series (UGI) to rule

TABLE 5.2 Tests for gastroesophageal reflux disease and motility problems

Study	Comments
Gastric pH; guaiac test	• Gastric pH typically 1.5-3.5; medications that reduce gastric acid secretion will increase the gastric pH • Guaiac test: identifies presence of blood
Upper gastrointestinal series (upper GI; barium swallow)	• Used to detect anatomical abnormalities of the GI tract • Not used to diagnose reflux • If a prior study has assessed anatomy, a repeat study is unlikely to provide new information that alters the care plan but will result in unnecessary radiation exposure
Esophageal pH probe	• Considered "gold" standard for diagnosing acid reflux • Will not detect non-acid reflux
Esophagogastroduodenoscopy (EGD; upper endoscopy)	• Requires sedation or anesthesia • Used to detect esophagitis resulting from acid reflux, eosinophilic esophagitis, gastric ulcers, or *Helicobacter pylori* infection
Multichannel intraluminal impedance study	• Measures impedance (the flow of liquids and gases in the esophagus) as well as pH • Able to detect acid as well as non-acid reflux
Gastric emptying scintiscan	• Used to measure the rate of emptying from the stomach • Standards not well established
Gastroesophageal scintigraph ("milk scan")	• Used to quantitatively detect reflux from the stomach into the esophagus and assess for the presence of aspiration • Not recommended for the routine evaluation of GERD
Manometry testing	• Detects pressure within the GI tract to evaluate the effectiveness of motility (movement in the GI tract) • Used to measure the strength, frequency, and coordination of peristalsis and contractions throughout the GI tract • Identifies intestinal myopathies (abnormal function of the muscles of the GI tract) and neuropathies (abnormal function of the nerves that regulate muscle contractions)

out an anatomical cause of symptoms, pH probe to assess for evidence of acid reflux, and endoscopy to assess for other disorders such as eosinophilic esophagitis. A typical approach is to identify clinical suspicion for GERD in a child who has SNI, obtain a UGI for the assessment of GI tract anatomy, and initiate empirical treatment with medications. It is not necessary to repeat UGI if a prior UGI identified normal anatomy. Information on tests for GERD and associated motility problems is summarized in table 5.2.

Medications

The mainstay of GERD treatment is medications that reduce gastric acid secretion: histamine-2 receptor blockers (H-2 blockers) and proton pump inhibitors (PPIs). Other drugs include those that buffer acid, such as antacids; those that provide a protective barrier, such as sucralfate; and prokinetics, which improve gastric emptying and intestinal motility (Böhmer et al. 2000; Cheung et al. 2001; Vandenplas et al. 2009).

Treatment can be started empirically, based on information from the child's history and a UGI series. PPIs are considered superior to H-2 blockers for the healing of erosive esophagitis and the relief of GERD symptoms (Vandenplas et al. 2009). When using PPIs, a three-month treatment course is recommended. A rebound effect can occur after a PPI is discontinued, as a result of transient increased gastric acid production. To minimize overuse of PPIs, rebound symptoms might be best managed with other, short-term or intermittent treatment options, such as sucralfate or antacids.

Potential risks associated with long-term use of PPIs include *Clostridium difficile*, small bowel bacterial overgrowth, pneumonia, bone fractures, and hypomagnesemia (Sheen and Triadafilopoulos 2011). Some children with recurrent symptoms may benefit from intermittent use of an H-2 blocker or PPI, or from daily treatment at a lower dose.

Prokinetic (promotility) medication options are limited and include metoclopramide and erythromycin (Chicella et al. 2005; Curry, Lander, and Stringer 2001; Hasler 2003; Sullivan 2008; Vandenplas et al. 2009). There is no information to suggest that metoclopramide is of greater benefit than erythromycin for the treatment of slow motility in children who have SNI. In addition, these drugs often have limited benefit. This may partially reflect the lack of recognition of other causes of vomiting and feeding intolerance in children who have SNI. At this time, there is insufficient evidence to recommend the routine use of prokinetic drugs for

GERD. If a trial is considered, erythromycin has the advantage of fewer adverse side effects.

Metoclopramide must be used with caution. As an antidopaminergic drug, it can result in extrapyramidal symptoms such as dystonic reactions, especially when used in children. The features of a dystonic reaction may be similar to other problems in children who have SNI, so it is important to be vigilant for this adverse reaction. The symptoms of a dystonic reaction include intermittent or sustained involuntary contractions of muscles in the face (grimacing, tongue protrusion, lip smacking, puckering of the lips, and rapid eye blinking), neck, trunk, and extremities, as well as appearing restless and agitated. Dystonic reaction is considered one of the most common causes of drug-induced movement disorders. Metoclopramide can also result in seizures or can lower the seizure threshold. It is approved for short-term use of 4 to 12 weeks and carries a black box warning by the U.S. Food and Drug Administration (FDA). Other problems associated with metoclopramide include irritability and permanent tardive dyskinesia (Hibbs and Lorch 2006; Vandenplas et al. 2009). Domperidone is an alternative used in Canada and Europe but is not available in the United States. It is considered safer than metoclopramide, as it does not easily cross the blood-brain barrier, though dystonic reactions can still occur (Steinherz et al. 1986; Tonini et al. 2004). These drug reactions probably reflect the increased risk of dystonic reactions in children and the potential for children to have a more permeable blood-brain barrier.

Other medications include bethanechol, a direct cholinergic agonist, with unproven benefit and prominent side effects. Adverse events include bronchoconstriction, salivation, abdominal cramping, bradycardia, and hypotension. For these reasons it is not recommended for routine use. Medications that are now being researched include 5HT-4 receptor agonists, which may be preferable because of the beneficial effect on motility.

If symptoms resolve with a PPI or other medication, we can reasonably assume that the symptoms were caused by GERD. Further testing should be considered when symptoms persist or return (table 5.2). This is always the time to ask the following questions:

- What will the test tell me that I do not already know?
- Will the test help determine treatment for the problem, or will it just document a problem?

- Have medication trials for other causes of retching and vomiting been considered?

Helicobacter pylori

Infection by *Helicobacter pylori* (*H. pylori*) can result in gastritis and peptic ulcer disease, though many people with *H. pylori* do not develop these conditions. There are several features that suggest infection with *H. pylori*:

- Recurrent "coffee-grounds" gastrostomy tube drainage
- Recurrent guaiac-positive gastrostomy drainage or stool
- GI bleeding
- Recurrent vomiting
- Irritability associated with feedings

In a study of children with neurological impairment, a significantly greater rate of *H. pylori* infection was identified in those residing in a long-term care facility than in those living at home (Proujansky et al. 1994). Symptoms resolved in 50% of children following treatment for *H. pylori*, including all children with a guaiac-positive test. In contrast, vomiting and irritability were more likely to persist after treatment in this group, indicating that *H. pylori* was not the cause of these symptoms and the need to consider other contributing problems.

When considering how to apply these guidelines for children who have SNI, some thought should be given to the recently published guidelines for diagnosis of *H. pylori* in children (Koletzko et al. 2011). Though endoscopy is recommended for diagnosis, this should be considered in the context of the risk associated with an invasive procedure in children with greater risk for complications. Noninvasive tests include *H. pylori* stool antigen, preferably using monoclonal antibodies; of note, recent guidelines for the general pediatric population recommend the use of this test for determining eradication of *H. pylori*. The ^{13}C-urea breath test (UBT) is another noninvasive test, though it is not always available. Testing for antibodies against *H. pylori* is not recommended, as the antibodies can remain in the blood, giving a positive test result, for months to years after an infection resolves. First-line treatment for children includes triple therapy with a PPI + amoxicillin + metronidazole, or a PPI + amoxicillin + clarithromycin, given for 10 to 14 days.

Anti-reflux surgery

Anti-reflux surgery (ARS) is beneficial for some children with chronic GERD and persistent vomiting, but must be pursued cautiously for children who have SNI. Compared with typically developing children, these children have a higher incidence of surgical failure, development of distressing symptoms, and mortality (Hament et al. 2001; Subramaniam and Dickson 2000). These outcomes probably reflect the under-recognition of visceral hyperalgesia and dysautonomia in some children, resulting in surgical treatment before treating these potential sources of symptoms.

Anti-reflux surgery is thought to prevent aspiration and thereby maintain respiratory health in children who have SNI, but studies suggest that ARS may not alter the long-term respiratory problems for some children, most likely reflecting multiple other factors not addressed by ARS (Bui et al. 1989; Cheung et al. 2006; Kawahara et al. 2004; S. L. Lee et al. 2008; Srivastava, Berry, et al. 2009). As covered in greater detail in chapter 6, these contributing factors can include chronic silent aspiration of secretions, impaired effectiveness of mucus mobilization, chronic shallow breathing, and the development of mucus plugs in the lungs.

Risks associated with ARS, especially for children who have SNI, include development of retching or worsening of preexisting retching (Antao et al. 2005; Richards et al. 1998; Richards et al. 2001). In addition, pain may develop or worsen following surgery to the intestinal tract. Following Nissen fundoplication in their children, parents reported higher levels of pain in response to the same degree of gastric distension (Complex Child E-Magazine 2009; Mousa et al. 2006). In addition, symptoms can worsen following ARS in children with slow motility of the GI tract. Symptoms that occur following ARS are sometimes referred to as "gas-bloat syndrome," including stomach and intestinal distension from gas as a result of the inability to belch. Other symptoms with "gas-bloat" include abdominal pain and retching—again, with an overlap in the symptoms seen with visceral hyperalgesia and dysautonomia. Mortality after ARS is higher in children who have SNI.

Considering these possible outcomes, thought should be given, prior to ARS, to an empirical medication trial directed at visceral hyperalgesia and dysautonomia, especially in children with retching and gagging or those with pallor and distress with vomiting (table 5.1; see also table 5.7). There may also be benefit in a medication trial directed at blocking the receptors

that trigger the vomiting reflex (see tables 5.4 and 5.5). ARS can be beneficial for some children, but a consideration of these other sources of symptoms can minimize the need for surgery in others.

Pyloroplasty

Gastric-emptying procedures are sometimes done in conjunction with ARS. This surgical intervention is typically considered for patients with delayed gastric emptying as assessed by gastric-emptying scintiscan. There are only a few studies reviewing the outcome following pyloroplasty, with variable results and conclusions (Bustorff-Silva et al. 1999; Dunn et al. 1998; Struijs et al. 2010). In addition, gastric-emptying scans may not be as informative as intended, with either no correlation between emptying time and reflux severity or inaccuracy in predicting the benefit from pyloroplasty (Khajanchee et al. 2009; Spiroglou et al. 2004).

Because the role of gastric-emptying scans and the benefit of surgical pyloroplasty are unclear, it is important to first consider the symptoms that suggest delayed gastric emptying. Such symptoms include retching, bloating, feeding intolerance, and discomfort. These symptoms can suggest other problems, however, including visceral hyperalgesia, stimulation of the vomiting reflex, autonomic dysfunction, and pseudo-obstruction. Empirical medication trials directed at these problems, as well as interventions such as jejunostomy (J-tube) feedings, should be considered before deciding on a surgical intervention with unclear benefit.

Gastrojejunal feeding tubes

Another option for management of persistent vomiting and other symptoms associated with GERD is placement of a gastrojejunal feeding tube (GJ tube). Use of a GJ tube allows feedings to bypass the stomach by directly entering the jejunum, the upper portion of the intestines. The goal is to eliminate feedings as a source of reflux. Medications can continue to be given through the gastric port of the tube, if tolerated.

The biggest downside of the GJ tube is the lost convenience of changing the tube at home, as can be done with a gastrostomy tube (G tube). In addition, jejunal feedings require continuous delivery of formula with the use of a feeding pump, adding to the inconvenience of extra equipment during transportation.

In a recent study comparing first fundoplication with first GJ-tube placement for the management of GER in neurologically impaired chil-

dren, outcomes were similar, including similar rates of aspiration pneumonia and mortality following both interventions (Srivastava, Downey, et al. 2009). In a retrospective review comparing complications, there was no significant difference in most complications between a G tube with fundoplication and GJ-tube placement (Wales et al. 2002). Retching was one of the few complications with a significant difference, with retching experienced by more than one in three (36.5%) of the patients with a G tube and fundoplication versus 17% of the patients with a GJ tube. There was a higher rate of tube breakage, blockage, and dislodgement in the patients with a GJ tube. This resulted in tube manipulation an average of 1.68 times per year for patients with a GJ tube. Four (8%) of the patients with a GJ tube went on to have Nissen fundoplication surgery. In another study, similar problems were identified with GJ tubes, including tube obstruction, tube migration, tube dislodgement, and intussusception (Friedman et al. 2004).

GJ tubes appear to be a reasonable alternative to fundoplication. They have the benefit of significantly less retching, despite the inconvenience of a higher incidence of tube-related problems. Another advantage of a GJ tube is the option of venting the gastrostomy port of the feeding tube even while feeding through the J-tube port. If the GJ tube is not meeting the identified goals of the intervention, it is convenient to switch back to a G tube while considering other management options.

Practical tips to minimize clogging of a J tube

The risk of tube blockage can be minimized with frequent flushing of the J-tube port. The most common recommendation is to flush the J tube with 10 to 30 mL of warm tap water every 4 to 6 hours, with a focus on daytime hours, as this procedure will not be routinely feasible overnight at home (Lord 2003; Smith and Myers 2005). Another option is to use a feeding pump with an automatic water flush feature. Less calorie-dense formula should be used when possible.

Medications are ideally given by G tube. When medications need to be given through the J tube, the tube should be flushed with 10 to 30 mL of water after stopping the formula, followed by the medication and another water flush. If more than one medication is being given, the recommended procedure is to flush with 5 mL of water between each drug. A liquid form of a medication should be used when possible. If a drug must be crushed, it is important that it be finely crushed and dispersed well in water. Enteric-coated, sustained-release, or time-release tablets or capsules cannot be given by G tube as they should not be crushed.

When a clog does occur, one cleaning method is to instill 30 to 50 mL of tepid water from a 60 mL syringe into the feeding tube. The syringe should be gently pulled back and forth in an attempt to dislodge the clog. Meat tenderizer, cranberry juice, or ginger ale or other soda should not be used. These have been found to be ineffective or to worsen the clog.

Another option is a pancreatic enzyme. These are medications used for patients with cystic fibrosis, to replace the enzymes not produced naturally. They may help unclog a J tube by breaking down proteins, starches, and fats. Immediate-release pancreatic enzymes are no longer available, and it is less clear whether the delayed-release enzymes are as effective at unclogging a J tube (Gillette, Knott, and Frohnapple 2011). One hospital reports that only 37% of tubes unclogged with a delayed-release enzyme (Kumpf 2012). One capsule of Zenpep or Creon is mixed with 5 mL of water and one-eighth of a teaspoon of baking soda, then instilled into the J tube; the tube is clamped for 30 minutes, and this is followed by a 15 to 30 mL water flush. It is unclear whether one enzyme strength is more effective than another. Another product is Clog Zapper, a kit that contains a syringe with a patented enzyme powder and a 12-inch hollow, small-diameter catheter that is inserted into the feeding tube (Lord 2003; Smith and Myers 2005).

Esophagogastric disconnection

Esophagogastric disconnection (EGD) is another surgical intervention that has been proposed for persistent GER. In two case series reviewing the use of EGD, there was a high rate of morbidity (30% to 43% early complications, 41% to 43% late complications) and mortality (22% to 29%) (Burrati et al. 2004; Danielson and Emmens 1999). Though the procedure was used to treat GER, some patients were noted before surgery to have retching, probably indicating a process distinct from GER. Medical and symptom management must be maximized before considering this surgical intervention, and any surgical intervention for GER must be considered cautiously for neurologically impaired children with retching, vomiting, and associated distress.

Summary of GERD and its treatment

GERD starts with a clinical suspicion, based on any of the following: irritability without a source, respiratory symptoms such as coughing and congestion, regurgitation, persistent vomiting, coffee-grounds appearance

of the content from emesis or from a G tube, vomiting of blood, and iron-deficiency anemia. A common approach once a clinical suspicion is identified is to obtain a UGI for the assessment of GI tract anatomy and to initiate a medication trial for gastric acid suppression (table 5.3). Improvement suggests that the presenting problems were caused by GERD. Further diagnostic studies can be considered when symptoms persist or return, despite normal findings on the UGI and a medication trial with a PPI or H-2 blocker. Other studies used in the evaluation of GERD and motility problems are summarized in table 5.2. This is also a time to consider other sources of the presenting symptoms (table 5.1).

Vomiting reflex and use of antiemetics

The vomiting reflex, also known as the emetic reflex, is a complex process that involves stimulation of the receptors in the vomiting center (VC), the final common pathway of the vomiting reflex. The VC is located in the medulla oblongata, an area of the brain involved in the autonomic regulation of respiration, heart rate, and blood pressure, as well as vomiting.

Information about the pathways that stimulate the VC is summarized in table 5.4, and the receptor targets for medications are summarized in tables 5.4 and 5.5. Recognizing these different pathways and the receptors involved can help guide treatment decisions. I focus here on the most likely sources to consider in children who have SNI. The receptors listed in tables 5.4 and 5.5 induce vomiting when stimulated. Medications that block these receptors then potentially block the stimulation of vomiting. The exception is 5HT-4, which when stimulated increases motility in the intestinal tract (rather than blocking the stimulation of receptors that induce vomiting).

Children who have SNI may be at risk for recurrent vomiting if there is increased activation or decreased inhibition of the CNS control of vomiting. In addition, the GI tract is a common source of stimulation of the VC. Input from the GI tract to the VC is predominantly mediated through the vagus and sympathetic nerves. The receptors include 5HT-3 receptors in the GI tract, D-2 receptors in the gastric wall, and 5HT-4 prokinetic receptors in the intestine. Substance P has also been identified in the wall of the GI tract; this is a neurotransmitter that induces vomiting through stimulation of the NK-1 receptors located in the chemoreceptor trigger zone.

Stimulation of these receptors in the GI tract involves either distension, as detected by mechanoreceptors, or inflammation of injured tissue in the GI tract, as detected by chemoreceptors. The GI tract may be distended

TABLE 5.3 Interventions for GERD and impaired motility

Intervention	Comments
Reduce gastric acid secretion	
Histamine-2 (H-2) receptor blockers: ranitidine (Zantac) Proton pump inhibitors (PPIs): omeprazole (Prilosec), lansoprazole (Prevacid); pantoprazole (Protonix)	• PPIs considered superior to H-2 blockers • Three-month treatment course recommended • Discontinuation of a PPI can result in a transient increase in stomach acid production; options for treating rebound symptoms include antacids, sucralfate, or an H-2 blocker • Theoretical risks associated with long-term use of PPIs: *Clostridium difficile*, small bowel bacterial overgrowth, pneumonia, and low magnesium level
Buffer stomach acid	
Antacids: Maalox, Milk of Magnesia Sucralfate (Carafate)	• Other options for short-term or intermittent treatment of symptoms resulting from stomach acid
Improve gastrointestinal motility	
Erythromycin Metoclopramide (Reglan)	• Caution with the use of metoclopramide, given the risk of dystonic reactions (sustained muscle contractions, with twisting, repetitive movement, and abnormal postures), restlessness, and nonspecific irritability; higher risk in children • Metoclopramide approved for short-term use, 4–12 weeks
Surgical interventions	
Anti-reflux surgery (ARS), also referred to as fundoplication Pyloroplasty Esophagogastric disconnection (EGD)	• ARS: surgical tightening of the junction between the stomach and esophagus in an attempt to prevent further reflux; can result in retching and visceral pain • Pyloroplasty: surgical widening of the pylorus (lower part of the stomach) to improve emptying into the duodenum (upper intestine); unproven benefit • EGD: esophagus disconnected from the stomach and reattached to the small bowel (intestine)

TABLE 5.3 *(continued)*

Intervention	Comments
	• Consider a trial of J-tube feeding before surgical interventions, as well as empirical medication trials for other sources of the presenting symptoms, including treatment of visceral hyperalgesia and use of antiemetics
Jejunostomy feeding tube	
Gastrojejunal feeding tube (GJ tube)	• Allows simultaneous venting of the G port and feeding through the J port
Address contributing problems	
Constipation	
H. pylori	• *H. pylori* suggested by recurrent "coffee grounds" content or blood in G-tube drainage; identified by stool antigen, endoscopy, or ^{13}C-urea breath test; treated with triple therapy
Problems with similar features	
Visceral hyperalgesia	• See table 5.1
Autonomic dysfunction	• Consider empirical trials such as gabapentin, cyproheptadine (Periactin), or ondansetron (Zofran)
Stimulation of the vomiting reflex	

due to impaired motility and have tissue injury from gastritis or GERD, for example. The goal is to treat sources when possible and block receptors when the source cannot be fully eliminated. The treatment of motility problems and use of antiemetics is intended to minimize the symptoms, as the primary motility disorder often cannot be "fixed" or removed.

Medications that block the receptors that stimulate the VC are listed in table 5.4. Many of the medications block one or more of the following receptors: serotonin (5HT-3 and 5HT-2), histamine (H-1), acetylcholine (Ach), and dopamine (D-2). As an example, cyproheptadine blocks more than one receptor involved with triggering the vomiting reflex.

The NK-1 receptor has received more recent focus. Aprepitant, an NK-1 receptor antagonist, is approved for treatment of chemotherapy-induced nausea and vomiting (CINV) and prevention of postsurgical nausea and vomiting (Curran and Robinson 2009; Gan et al. 2007). It is also being considered for other causes of vomiting such as cyclical vomiting syndrome

TABLE 5.4 Mechanisms that stimulate the vomiting reflex

Sites	Causes	Receptors/mechanisms	Therapeutic agents
Central sites			
Vomiting center (VC), located in the medulla oblongata of the CNS	Final common pathway stimulated by the other sites listed	Histamine (H-1)	Antihistamines (diphenhydramine, cyproheptadine)
		Acetylcholine (Ach)	Anticholinergics (scopolamine, cyproheptadine)
		Serotonin (5HT-2)	5HT-2 antagonists (cyproheptadine, levomepromazine)
Chemoreceptor trigger zone (CTZ)	Medications (chemotherapy, opioids, antibiotics, anticonvulsants)	Serotonin (5HT-3)	5HT-3 antagonists (ondansetron, granisetron)
	Metabolic imbalance (hyponatremia, hypercalcemia, uremia, ketoacidosis)	Dopamine (D-2)	Butyrophenones (haloperidol, droperidol)
			Phenothiazines (prochlorperazine, chlorpromazine)
		Neurokinin (NK-1)	NK-1 antagonists (aprepitant)
Vestibular nucleus	Disorders of the vestibular nucleus and cranial nerve VIII	Histamine (H-1)	Antihistamines (diphenhydramine, promethazine)
		Acetylcholine (Ach)	Anticholinergics (scopolamine, hyoscyamine)

Meningeal mechanoreceptors	Increased intracranial pressure, tumor, infection	Stimulation of VC	Corticosteroids
Cortex	Anxiety	Stimulation of CTZ and VC	Relaxation techniques, benzodiazepines, dronabinol
Gastrointestinal sites			
Mechanoreceptors (detect distension) Chemoreceptors (detect inflammation and tissue injury)	Slow motility such as caused by drugs (anticholinergics, opioids), constipation, autonomic dysfunction, esophagitis, gastritis, distension of stomach or intestines, distension or inflammation of gallbladder	Vagus nerve afferents (nerve signals from the gut to the brain) Histamine (H-1) Serotonin (5HT-3)	H-2 blocker (ranitidine) Proton pump inhibitor (omeprazole) Prokinetic agents (erythromycin, metoclopramide) Antihistamines (diphenhydramine, promethazine) 5HT-3 antagonists (ondansetron, granisetron)

TABLE 5.5 Summary of the receptor targets for the treatment of retching and vomiting

Receptors	Medications	Comments
5HT-2, 5HT-3, H-1, Ach, D-2, NK-1	Medications that block these receptors (antagonists): Cyproheptadine (5HT-2, H-1, Ach) Ondansetron (5HT-3) Haloperidol (D-2) Aprepitant (NK-1)	• Receptors that, when stimulated, result in vomiting • Medications that block these receptors may decrease retching and vomiting • Risk of dystonic reaction with haloperidol • Aprepitant approved only for chemotherapy-induced vomiting
C-1, C-2	Medications that stimulate these receptors (agonists): Dronabinol	• Most studied for chemotherapy-induced vomiting and as appetite stimulant • Not studied in children who have SNI • Side effects include irritability, restlessness, delayed gastric motility
5HT-4	No medications (receptor agonists) currently available	• Stimulation of receptor increases motility in the intestinal tract

(Abell et al. 2008). There are limited studies on aprepitant use in children, and only in those with CINV (Gore et al. 2009).

There are currently no drugs available in the United States that stimulate the 5HT-4 receptor, though this remains an area of investigation, given the beneficial effect on motility. Other drugs include dronabinol, best studied and approved for use in CINV and for anorexia (loss of appetite) secondary to AIDS (Grotenhermen 2005). Dronabinol also appears to improve appetite stimulation. It is a cannabinoid receptor (CB-1 and CB-2) agonist that stimulates the CB-1 and CB-2 receptors located in the CNS, peripheral nervous system, and elsewhere. Side effects such as anxiety, depression, irritability, restlessness, and delayed gastric motility can limit its use.

In summary, medications to consider for trials include cyproheptadine and ondansetron. Medications that block the D-2 receptor can also have a role, though the risk of a dystonic reaction limits their use for children who have SNI. As noted, there are currently no medications that stimulate the 5HT-4 receptor, but this remains an area of investigation, given the beneficial effect for intestinal motility.

Retching in children who have SNI

Children who have SNI may be at risk for retching as a result of increased activation or decreased inhibition of the central control of vomiting (Sullivan 2008). Such children can also develop or continue retching following Nissen fundoplication (Richards et al. 1998; Richards et al. 2001; Zangen et al. 2003).

Alimemazine, a phenothiazine derivative, was found to significantly reduce retching that developed in children with SNI following Nissen fundoplication (Antao et al. 2005). Though alimemazine is not available in the United States, the overlap in receptor-blocking properties with cyproheptadine, which blocks the 5HT-2, H-1, and Ach receptors, forms the theoretical basis for using cyproheptadine to treat retching for children who have SNI. These properties are also similar to those of the antiemetic levomepromazine, which blocks the 5HT-2, H-1, Ach, and D-2 receptors, used in Europe to treat nausea and vomiting (Antonarakis and Hain 2004).

Medications play a useful role in blocking stimulation of the vomiting reflex in children who have SNI and associated retching and/or vomiting. Recognizing the receptors involved in stimulation of retching and vomiting allows empirical selection of medications that block these specific receptors. As with pain, it is not always possible to eliminate the source of retching and vomiting, but an empirical trial can often find a drug to lessen the distress from such symptoms.

William is a 34-year-old who has cerebral palsy resulting from anoxia at birth, caused by a maternal hemorrhage. He has experienced persistent daily retching that is associated with vomiting and appearing distressed, with tears. Findings on endoscopy, colonoscopy, and abdominal CT scan have been normal. Interventions, including feedings by J tube, management of constipation, and medications including metoclopramide, a PPI, and prochlorperazine, have provided no benefit. William has complete resolution of symptoms with cyproheptadine and is described as "doing exceptionally wonderful!"

Andy, a 25-year-old who has cerebral palsy resulting from a structural CNS abnormality, has a long history of daily retching "that can be heard across the room." Evaluation has given unremarkable findings, including abdominal ultrasound and CT scan. Interventions have provided limited benefit, including J-tube feeding, PPI, H-2 blocker, ondansetron, and treatment for small bowel

bacterial overgrowth. A trial of cyproheptadine is initiated, with complete resolution of retching, and Andy remains symptom free 10 months later.

Hailey is a 7-year-old girl who has a genetic disorder with associated SNI. She has daily vomiting despite treatment with an H-2 blocker, PPI, change in formula and feeding rate, and Nissen fundoplication. Her mother minimizes moving Hailey, as this is a trigger for vomiting, described as "like motion sickness." Her vomiting is forceful, with gagging and retching at other times. Her vomiting also limits the amount of formula she can tolerate. A cyproheptadine trial results in significant improvement, including weight gain. As described by her mom, "I can now take her with us outside the house without her vomiting when I move her; she is like a new kid."

The role of antispasmodics

The GI antispasmodic drugs such as dicyclomine and hyoscyamine have uncertain effectiveness. As anticholinergics (Ach receptor blockers), they are thought to relieve GI spasm through antimuscarinic action on parasympathetic innervations. They have been mostly studied for symptom relief in irritable bowel syndrome (Hasler 2003). Side effects include constipation, dry mouth, and urinary retention. These medications should be avoided if a patient is taking cyproheptadine, which also blocks the Ach receptor, and they are unlikely to add benefit if cyproheptadine has already been used.

Visceral hyperalgesia

Visceral hyperalgesia is an altered response to visceral stimulation, resulting in a decreased activation threshold for symptom generation in response to a stimulus, such as distension of the intestines (Delgado-Aros and Camilleri 2005). Symptoms include retching and vomiting as well as pain localized to the GI tract. (This topic is also covered in chapter 4.)

Visceral hyperalgesia was identified as the source of retching and vomiting in 12 of 14 medically fragile children with symptoms that persisted following treatment of GERD with medications and Nissen fundoplication (Zangen et al. 2003). Tricyclic antidepressants (TCAs), gabapentin, cyproheptadine, and dicyclomine were used in various combinations, based on evaluation results. Following treatment, there was a significant decrease in the average number of retching episodes per day, from 14 to 1.5, with 11 children reported as "better" or "much better." The authors speculated that repeated painful stimulation of the GI tract could lead to sensitization

and development of visceral sensory dysfunction. Children who have SNI have an increased frequency of problems that could sensitize the intestines, such as GERD, G-tube placement, anti-reflux surgery, and distension due to constipation (Del Giudice et al. 1999; Schwarz et al. 2001). As described in more detail in chapter 4, treatment of visceral hyperalgesia includes gabapentin, pregabalin, and nortriptyline (Delgado-Aros and Camilleri 2005; Hasler 2003; Houghton et al. 2007; K. J. Lee, Kim, and Cho 2005; Zangen et al. 2003). The cases of Dylan and Lars, in chapter 4, illustrate improvement in both vomiting and pain localized to the GI tract following the use of gabapentin and nortriptyline.

Symptoms that may suggest visceral hyperalgesia in nonverbal children who have SNI (as well as suggest the visceral symptoms associated with central neuropathic pain) include the following:

- Pain, retching, or vomiting associated with G-tube feedings, suggesting a decreased stomach volume threshold for symptom generation
- Pain associated with intestinal gas and J-tube feedings, suggesting pain when the intestines are normally distended
- Pain associated with bowel movements and passing gas, suggesting pain associated with distension of the colon
- A response out of proportion to a stimulus, such as prolonged and excessive crying spells associated with intestinal gas, constipation, or GERD

Autonomic dysfunction

Autonomic dysfunction, also referred to as dysautonomia, results in alterations of the autonomic function of many organs. (This topic is covered in greater detail in chapter 7.) In addition to the hypothalamus, areas in the brain involved in regulation of the autonomic nervous system include the medulla oblongata, which includes the vomiting center.

Problems described in children who have dysautonomia include the following (Axelrod and Berlin 2009; Chelimsky and Chelimsky 2001; Chelimsky, Hupertz, and Chelimsky 1999):

- Alterations in heart rate and body temperature
- Pallor or flushing of the face and body
- Retching, vomiting, impaired intestinal motility, and constipation
- Urinary retention
- Abnormal sweating

- Increased saliva production
- Arching and agitation

For children able to describe their symptoms, autonomic dysfunction is also said to be a source of generalized discomfort and abdominal pain.

There is a significant overlap between these symptoms and the symptoms associated with activation of the vomiting reflex, which can include retching, vomiting, sweating, pallor, increased salivation, increased heart rate, and agitation. A limited number of case reports suggest some benefit from cyproheptadine for patients with dysautonomia that includes retching and/or hypothermia (Kloos 1995; Ruiz et al. 2003; Sheth, Barron, and Hartlage 1994). Other medications used to treat dysautonomia include gabapentin, pregabalin, and clonidine (Axelrod and Berlin 2009; Baguley et al. 2004; Baguley et al. 2007).

Intestinal pseudo-obstruction

Intestinal pseudo-obstruction, also referred to as Ogilvie syndrome, is a clinical syndrome caused by ineffective intestinal propulsion characterized by features of intestinal obstruction but in the absence of any evidence of an occluding lesion of the intestinal tract. Features of pseudo-obstruction include abdominal distension, pain, vomiting, and severe constipation. X-rays demonstrate intestinal distension. Patients at risk include children who have mitochondrial disorders or conditions with significant autonomic dysfunction. Initial management is supportive:

- Withholding tube feedings
- Venting of a G tube
- Providing IV fluid
- Correcting electrolyte abnormalities
- Discontinuing medications that slow intestinal motility, when possible
- Using a rectal tube for decompression of the colon

Neostigmine, an acetylcholinesterase inhibitor, is beneficial for patients with acute intestinal pseudo-obstruction that fails to resolve with supportive therapy (Ponec, Saunders, and Kimmey 1999). This drug must be used with caution because of its potential cholinergic side effects, including bradycardia, hypotension, bronchoconstriction, increased salivation, and increased bronchial secretions. Glycopyrrolate has been suggested for use

in conjunction with neostigmine to minimize the effects of bradycardia. A test dose of 0.01 to 0.02 mg/kg (maximum starting dose 1 mg) can be given intravenously over 3 minutes in the hospital, with monitoring, titrated up to a dose of 0.08 mg/kg if needed.

Neostigmine was reported as effective for one child with cerebral palsy and a clinical picture of prolonged ileus in the postoperative period. A starting dose of 0.007 mg/kg was used, titrated up to a dose of 0.05 mg/kg, resulting in large stool output and a significant reduction in abdominal distension after 3.5 hours (Gmora, Poenaru, and Tsai 2002). Another case report found daily oral neostigmine to be beneficial, after first establishing benefit with an IV dose, for a patient with a mitochondrial I/III complex deficiency and frequent hospitalizations for feeding intolerance, abdominal distension, and worsening seizures (Gilles 2011). The oral equivalent is calculated as approximately 15 mg oral to 0.5 mg IV, given the low absorption of the oral form. The use of subcutaneous neostigmine started at a lower dose has also been reported, with a case series of eight adult patients treated with a median dose of 0.5 mg (range 0.25 to 1.25 mg) (Rubiales et al. 2006).

Pyridostigmine is another medication that produces cholinergic activity. It has been reported to benefit patients with recurrent pseudo-obstruction. In one case series, all seven patients with pseudo-obstruction had relief of symptoms, starting with a low dose of 10 mg twice per day (BID) given by mouth. If there was no benefit, doses were increased by 10 mg, with the effective dose ranging from 10 to 30 mg BID. An extrapolated initial dose to consider for pediatric patients is 0.2 mg/kg, much lower than the treatment dose used for myasthenia gravis (O'Dea, Brookes, and Wattchow 2010).

Children with significant recurrent episodes of intestinal pseudo-obstruction may benefit from as-needed neostigmine or pyridostigmine, once a dose has been established, but this warrants further study. A decision about a medication trial should weigh the risks and benefits of treatment against the significance of recurrent intestinal pseudo-obstruction.

Erythromycin is also of benefit for some patients with intestinal pseudo-obstruction, according to several case reports (Emmanuel, Shand, and Kamm 2004; Jiang et al. 2007). Though it is unclear which patients will benefit, this is a safe medication for an empirical trial. Other medications that have been considered include 5HT-4 receptor agonists and somatostatin analogues such as octreotide.

A final consideration is the higher risk of mortality associated with life-threatening episodes of intestinal pseudo-obstruction. Mortality has been reported to be 20% to 30% (Delgado-Aros and Camilleri 2003; Goulet et al.

1999; Heneyke et al. 1999; Jancar and Speller 1994). It is unclear whether surgery provides a better outcome than conservative management.

Constipation

Constipation is a common if not universal problem among children who have SNI. Such children have many reasons to be at risk for constipation, including low fiber in the diet, lack of walking and standing, slow GI motility, central hypothyroidism, and autonomic dysfunction. In addition, a child may be taking a medication that is slowing intestinal motility, including anticholinergics, opioids, and benzodiazepines. Constipation can contribute to other sources of vomiting and retching by slowing intestinal motility. It also contributes to visceral hyperalgesia by increasing distension in the colon. Treatment of constipation is essential to keep it from contributing to other problems.

Management starts with a review of treatable contributing problems. This includes, when possible, stopping medications that can contribute to constipation. In addition, children who have SNI are at an increased risk for hypothyroidism. One approach is to obtain thyroid function blood tests yearly so as to identify this condition before the symptoms associated with hypothyroidism, including constipation, become significant.

Dietary management includes sufficient water intake and use of a formula containing fiber. Treatment involves understanding the mechanisms of different interventions (table 5.6). Some children benefit from more than one approach, such as the use of an oral osmotic agent with as-needed magnesium hydroxide, suppository, or enema. Symptoms associated with treatment can include increased intestinal gas, such as with lactulose, and intestinal cramping from interventions that stimulate peristalsis. Chronic use of senna may damage the myenteric plexus, though this remains unclear. In general, senna is not recommend for long-term use. The fear of dependency on suppositories or enemas is probably not warranted. They remain effective when used as needed, with the goal being to maintain a bowel movement every day to every other day.

Other problems contributing to vomiting

Medications

Medications are important to consider as possible causes of vomiting. Some medications contribute to retching and vomiting by slowing intestinal motility; these include dicyclomine, hyoscyamine, diphenhydramine,

TABLE 5.6 Interventions for constipation

Intervention	Mechanism of action
Polyethylene glycol (Miralax)	Osmotic (stimulates peristalsis through strong osmotic effect)
Lactulose	Osmotic (retains water in intestines, causing distension and peristalsis)
Magnesium hydroxide (Milk of Magnesia)	Osmotic (retains water in intestines, causing distension and peristalsis)
Senna liquid (Senokot)	Stimulant (causes peristalsis)
Glycerin suppository	Lubricant
Bisacodyl suppository (Dulcolax)	Stimulant (causes peristalsis)
Sodium phosphate enema (Fleet)	Osmotic (draws water into stool, stimulating peristalsis)
Docusate enema (Enemeez)	Stool softener (surfactant)

cyproheptadine, ranitidine, TCAs, scopolamine, glycopyrrolate, and oxybutynin. Other medications can be more directly irritating to the intestinal tract, such as nonsteroidal anti-inflammatory drugs (NSAIDs) and certain anticonvulsants (valproic acid, carbamazepine, and zonisamide).

Respiratory secretions

Respiratory secretions and mucus seem to be another factor contributing to vomiting, as commonly reported by families. Gagging, retching, and vomiting often occur in the morning, with parents seeing mucus in the expelled content. For some children, this is the only time they vomit; for these children, a focus on interventions that assist with clearing of chronic secretions is the most beneficial approach.

Systemic illness

Children who have SNI and intermittent GI problems may experience an increase in symptoms of feeding intolerance during an acute illness, such as a respiratory exacerbation. When ill, such a child may have retching, vomiting, and inability to tolerate the usual feeding schedule. For a child who is well nourished, one simple approach is to provide hydration

through the feeding tube in the form of an electrolyte solution for 24 to 36 hours, and then resume formula feeding. At a time of illness, a person often has a decreased appetite; a focus on fluids at such times is an appropriate approach.

Summary of the management of retching and vomiting

For the child with new-onset retching and vomiting, a medical review is needed to assess for common causes, such as viral infections of the GI tract and bladder infections, and less common but more serious causes, such as pancreatitis and bowel obstruction. For symptoms that persist after the initial evaluation, treatment of GER and constipation is an important initial step, because these problems are common and often chronic. A comprehensive history can disclose information to suggest other sources (table 5.1). Such problems and associated symptoms can include dysautonomia (retching, tachycardia, sweating, and flushing), activation of the vomiting reflex (retching, forceful vomiting, pallor, and sweating), and visceral hyperalgesia (retching and pain). Empirical medication trials can target these and other contributing problems (table 5.7).

I have provided here an overview of the available interventions for the problem of persistent retching and vomiting. The evidence to guide decisions is limited, however, so care must be taken not to introduce too many trial options. It is not necessary or "required" that all interventions be used when symptoms persist. For example, if medication trials have included cyproheptadine, there is no need to also initiate dicyclomine, given that both medications have anticholinergic properties. Instead, if symptoms remain intractable, it is beneficial to review how comprehensive prior evaluations and interventions have been. This helps lessen the fear that "we need to keep looking until we find the problem" and allows the healthcare team to consider the difference between "failure of the evaluation" and "failure of the body." Though vomiting is a less common problem than a decline in respiratory health in a child who has SNI, persistent vomiting is very distressing for both families and healthcare teams, as reviewed at the end of this chapter.

OTHER GI PROBLEMS AND PROBLEMS OF THE URINARY TRACT

Other potential problems in the abdominal organs of children who have SNI include pancreatitis, gallstones, diarrhea, small bowel bacterial

TABLE 5.7 Interventions for retching, vomiting, and associated discomfort

Intervention	Potential benefit/comments
Treat constipation (table 5.6).	• Minimizes colon distension and further slowing of motility
Identify medications that slow intestinal motility; decrease dose or discontinue when possible.	• Medications to consider include dicyclomine, hyoscyamine, diphenhydramine, cyproheptadine, ranitidine, TCAs, scopolamine, glycopyrrolate, and oxybutynin
Histamine-2 blockers (H-2 blockers) Proton pump inhibitors (PPIs) Sucralfate Antacids	• Reduce gastric acid production (H-2 blocker or PPI) • Provide a protective barrier in the stomach (sucralfate) • Neutralize gastric acid intermittently (antacids) • Ideally, PPI used for 12 weeks • Chronic use of PPIs is associated with *C. difficile*, small bowel bacterial overgrowth, pneumonia, bone fractures, and low serum magnesium (hypomagnesemia) • Anticipate transient rebound of gastric acid production when a PPI is stopped; consider managing with short-term use of antacids or sucralfate
PPI + amoxicillin + metronidazole	• Triple therapy for *H. pylori* infection identified by stool antigen or biopsies from endoscopy
Gabapentin, pregabalin	• Treatment of visceral hyperalgesia and dysautonomia
Nortriptyline (a TCA)	• Treatment of visceral hyperalgesia
Cyproheptadine (Periactin)	• Blocks 5HT-2, H-1, and Ach receptors involved in stimulation of the vomiting center in the CNS
Ondansetron (Zofran)	• Blocks 5HT-3 receptor involved in stimulation of the vomiting reflex
Erythromycin Metoclopramide (Reglan)	• May improve gastric emptying and intestinal motility • No clear benefit of one over the other, though erythromycin is safer than metoclopramide • Ideally, limit use of metoclopramide to 4–12 weeks

(continued)

TABLE 5.7 *(continued)*

Intervention	Potential benefit/comments
	• Monitor for signs of dystonic reaction with metoclopramide, including intermittent or sustained involuntary muscle contractions of the face (grimacing, tongue protrusion, lip smacking, puckering of the lips, rapid eye blinking), neck, trunk, and extremities; appearing restless or irritable • Increased risk of seizures with metoclopramide
Hyoscyamine (Levsin) Dicyclomine (Bentyl)	• Ach receptor blockers (anticholinergics) • Unclear benefit for GI tract spasms • Do not use if patient is taking cyproheptadine or other Ach blockers
G-tube venting and equipment that allows venting during feedings (Farrell)	• Minimizes gastric distension and associated discomfort
Gastrojejunal tube (GJ tube)	• Eliminates gastric distension and reflux resulting from formula feeding • G-tube venting possible while feeding through the J tube • GI pain may not improve with J-tube feedings
Elemental formula (e.g., Neocate, EleCare, Nutramigen)	• Anecdotal parental reports of benefit
Metronidazole (Flagyl) or rifaximine	• An empirical trial for small bowel bacterial overgrowth in children with persistent diarrhea (first check for liquid medications that contain sorbitol or lactulose)
Neostigmine or pyridostigmine Erythromycin	• Consider for a child with recurrent episodes of pseudo-obstruction, after ruling out a mechanical obstruction
Anti-reflux surgery (fundoplication)	• Consider empirical medication trials for problems outlined above before elective surgery • Greater benefit for persistent GI problems; less benefit for long-term respiratory decline in children with multiple contributing problems • Some children will develop retching, bloating, and discomfort following fundoplication

overgrowth, bladder dysfunction, urinary tract infection, and renal stones. The problem of persistent feeding intolerance is addressed later in the chapter.

Acute pancreatitis

Though pancreatitis is relatively uncommon in children who have SNI, such children have several risks for developing this condition. Recognizing these associated risks can help with diagnosis and minimize the risk of recurrence.

Risk factors for children who have SNI include medications, most commonly valproic acid, and hypothermia due to hypothalamic dysfunction with impaired temperature regulation. Hypothermia as a cause of pancreatitis is suggested by a case series of six children with SNI who developed acute pancreatitis, all with hypothermia and no other cause to explain development of the pancreatitis (Hauer 2008). Efforts to maintain the children's body temperature above 95 °F were associated with no further development of pancreatitis. Use of a hat, scarf, gloves, thick socks, and blankets is often effective at meeting the goal of maintaining body temperature above 94 to 95 °F. Hypothermia seems to be an infrequent cause of pancreatitis and probably requires significant hypothermia for a prolonged period, such as less than 92 °F for more than 8 hours. Cyproheptadine may be of benefit for some patients in minimizing centrally mediated hypothermia, based on a few case reports (Kloos 1995; Ruiz et al. 2003; Sheth, Barron, and Hartlage 1994).

Presenting signs and symptoms that suggest acute pancreatitis include increasing pain, irritability, vomiting, feeding intolerance, fever, and a tender abdomen. Initial management includes discontinuing tube feedings, providing IV fluids, and monitoring for complications. In addition, the child is evaluated to determine the reason for developing acute pancreatitis.

Gallstones

As with pancreatitis, gallstones are uncommon, but some children who have SNI may be at risk. Risk factors may include prolonged tube feeding, with resulting insufficient gallbladder emptying. A well-documented cause of gallstones is the prolonged use of IV nutrition (total parenteral nutrition, or TPN). Some children have diseases that increase the risk for development

of gallstones, including Rett syndrome and metachromatic leukodystrophy (MLD).

When gallstones are identified in children who have SNI, one of the challenges is determining when to surgically intervene. Surgical removal of the gallbladder is certainly necessary when it is inflamed or infected as a result of the gallstones. In contrast, gallstones can be monitored clinically when there are no associated symptoms or inflammation of the gallbladder.

Tim is a 22-year-old who has cerebral palsy. He is fed by G tube. He has been noted to have persistent pain behaviors despite treatment for GERD and constipation. Further studies include an ultrasound that identifies gallstones. Despite laparoscopic removal of the gallbladder, Tim continues to have pain behaviors weeks after surgery. Gabapentin is initiated at the recommendation of a pediatric palliative care physician, with improvement in pain symptoms within 1 week. In retrospect, no gallbladder wall thickening was found and the results of blood tests, including liver enzymes, total bilirubin, and alkaline phosphatase, were normal; this increases the possibility that the gallstones were an incidental finding and were not causing Tim's pain.

This case illustrates the challenge of weighing the risk associated with gallstones against the possibility that gallstones are not always the source of persistent discomfort in individuals who have SNI. In Tim's case, treatment with gabapentin as an intervention for central pain / visceral hyperalgesia may have addressed the primary source of his pain behaviors. However, information that indicated inflammation (cholecystitis) or infection of the gallbladder would indicate gallstones as the source of pain, as well as a condition that threatened the individual's health. Information to assist with clinical decision making includes ultrasound identification of gallbladder wall thickening or fluid collection, evidence of systemic illness such as fever, and elevated white blood cell count, liver enzymes such as alanine aminotransferase (ALT), total bilirubin (t bili), alkaline phosphatase (alk phos), and inflammatory markers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). For any child with evidence of inflammation or infection of the gallbladder, surgical removal would be warranted. Such challenges are best discussed with a healthcare team representing different expertise and experience, and ideally including a gastroenterologist, a pediatric surgeon, and a clinician involved in the long-term care of the child (to offer the perspective of the child's health baseline over time).

Even when there are no data to suggest inflammation or infection of the gallbladder, gallstones still pose a future risk. Decisions then must weigh the risk and benefit of clinical monitoring with consideration of surgical removal in the context of the child's overall health status. As an example, a child with Rett syndrome and no decline in health may have a greater lifetime risk of developing a diseased gallbladder. In contrast, if a child with MLD (a degenerative disease of the central and peripheral nervous systems, with a risk of gallstones developing from sulfatide accumulation) has experienced a significant decline in health, the risk of surgery may outweigh the risk of monitoring the child clinically. As reviewed earlier in this chapter and in chapter 4, other sources of the symptoms that prompted an evaluation need to be considered and treated.

Diarrhea

Diarrhea is defined as an excessive passing of unformed or liquid stool. Though it occurs less commonly than constipation in children who have SNI, it can become a problem for some children. Common causes of diarrhea include frequent antibiotic use, *Clostridium difficile* (C. diff.), liquid medications in a sorbitol base (Feldstein 1996), magnesium-containing antacids, and small bowel bacterial overgrowth.

Formula is not considered a significant factor in chronic diarrhea; other factors are more often identified (Heimburger, Sockwell, and Geels 1994). In one study looking at the role of formula in diarrhea, medications were the identified cause in 61% of patients, including sorbitol in liquid medications or repeated use of antibiotics (Edes, Walk, and Austin 1990). Interventions include changing to a formula with fiber, searching for the causes identified above, and considering other causes of chronic diarrhea as indicated by associated findings.

Jenny is a 10-year-old who has SNI and persistent diarrhea, typically with three to four loose stools per day. Studies for causes have produced negative findings, including stool cultures. Interventions have not provided benefit, including changes in her formula, a decrease in her thyroid replacement dose, and an empirical trial of metronidazole for small bowel bacterial overgrowth. Jenny's medications are reviewed, and the addition of liquid calcium glubionate (Neo-Calglucon) 6 months ago is noted. This is found to be giving 3 grams of sorbitol each day. One week after changing to a chewable calcium supplement, crushed and given by G tube, her stool frequency decreases to an average of one per day.

Small bowel bacterial overgrowth

Slow motility of the intestinal tract can result in small intestinal bacterial overgrowth (SIBO). Normally, the small bowel is relatively free of bacteria. SIBO is an excessive number of bacteria in the small intestine or in a blind loop of bowel. If the suspicion of bacterial overgrowth is high enough, the best diagnostic test is a treatment trial. If the symptoms improve, a presumed diagnosis of bacterial overgrowth can be made.

Symptoms of SIBO include nausea, excessive gas, distension of the abdomen, abdominal pain, and chronic diarrhea. The main feature distinguishing SIBO from other causes of nausea and pain may be diarrhea. In a child who has SNI, the presence of diarrhea along with pain and excessive gas may help determine when to consider empirical treatment for SIBO. Antibiotics are the mainstay of treatment, though this has been studied mostly in adults. Antibiotics include metronidazole, amoxicillin-clavulanate, and rifaximin, typically given for 7 to 10 days (Quigley and Abu-Shanab 2010). Some patients with recurrent symptoms benefit from a 5- to 10-day antibiotic course given monthly, rotating the antibiotics used. More specific testing to diagnose SIBO may be warranted for such patients. Diagnostic tests include the hydrogen breath test and D-xylose test. The usefulness of probiotics—bacterial preparations that beneficially alter the bacterial flora in the bowel—in treating bacterial overgrowth remains unclear.

Urinary tract: bladder dysfunction, urinary tract infection, and renal stones

Children who have SNI are at increased risk for urinary tract dysfunction. Problems can include retention of urine in the bladder, including residual urine after voiding; bladder distension; and urinary tract infection. Retention of urine can increase the risk of a UTI (also referred to as a bladder infection). In addition, constipation can result in or worsen urinary retention.

Some children benefit from a formal evaluation of the process of urine voiding from the bladder. The need for evaluation can be suggested by repeated UTIs or prolonged time intervals between voiding. Urologists are experts at assessing the function of the bladder, with the use of urodynamic tests such as cystometrogram (CMG). Interventions to manage alterations in voiding include intermittent urinary catheterization (cathing),

in which a sterile catheter is inserted into the bladder via the urethra. Intermittent cathing can decrease the risk of a UTI in those with retention of urine in the bladder.

Symptoms of a UTI in a nonverbal child who has SNI include new-onset pain, fever, strong-smelling urine, and vomiting. When a UTI is suspected, a urinalysis (UA), with culture of a sample obtained by sterile catheterization, is indicated. A UTI is suspected when a UA is positive for leukocyte esterase and/or nitrite and there are more than 10 white blood cells per high-power field. A urine culture is significant when the colony count of bacteria is greater than 100,000/mL. Some children, especially those with bladder dysfunction, have urine that is colonized with bacteria and will have a positive culture result in the absence of infection. A UA can distinguish a positive urine culture that indicates infection rather than colonization. Reserving treatment for when the UA indicates an infection can minimize overuse of antibiotics and subsequent antibiotic resistance. Prophylactic antibiotics are not routinely recommended for children with recurrent UTI, given the increase in antibiotic resistance (Conway et al. 2007).

Some children who have SNI are at risk for developing renal (kidney) stones, also referred to as nephrolithiasis or urolithiasis (McKay 2010). Kidney stones are suspected when there is blood in the urine, pain, and stones in the diaper, though they can be present with no symptoms. Tests to identify the presence of kidney stones are renal ultrasound or CT scan.

Risk factors for the development of stones include the ketogenic diet, recurrent UTI, and the medications zonisamide and topiramate. A significantly higher rate of renal stones was found in nonambulatory, neurologically impaired children who were taking topiramate. In this retrospective review, 54% of the children receiving topiramate developed clinical evidence of renal stones after a mean duration of 36 months (Goyal et al. 2009). This is significantly higher than the overall population risk of 1.5% to 5.6% reported for topiramate. Other factors may contribute in nonambulatory children who have SNI, including calcium and vitamin D supplementation in excess of need and calcium reabsorption from bone, all of which increase calcium excretion in the urine (Daudon and Jungers 2004; Goyal et al. 2009).

Children at risk for or identified as having renal stones benefit from an increase in fluid intake. Some stones contain calcium and form when the calcium level in the urine is high. Measuring urine calcium and creatinine levels can identify elevated calcium excretion in the urine, indicated by a urine calcium-to-creatinine ratio exceeding 0.2 mg/mg (0.56 mmol/mmol). Other tests of the urine are often obtained (McKay 2010). Thiazide diuretics

such as chlorothiazide (Diuril) are sometimes used to reduce the amount of calcium excreted by the kidneys into the urine. Thiazides also cause potassium (K^+) loss in the urine.

Analysis of stones found in the diaper can identify the type of stone and guide treatment. Some stones, such as *calcium oxalate* and *uric acid*, form when the urine is acidic (lower pH identified by UA). Potassium citrate (Polycitra) can increase the urine pH (make it more alkaline) and can replace potassium loss if a thiazide diuretic is used. In addition, citrate in the urine inhibits calcium oxalate formation. In contrast, *calcium phosphate* and *struvite* stones form when the urine is more alkaline ($pH > 6.5$ to 7). Potassium citrate should not be used for patients with these stones. Struvite stones form as a result of certain bacteria in the urine, including *Proteus*, *Klebsiella*, *Serratia*, and *Pseudomonas*. Identification and treatment of UTIs is important in the prevention of struvite stones.

Ultrasound and CT scans can detect the presence of stones, determine whether stones are causing obstruction and blocking the flow of urine, and monitor identified stones over time. Urologists and nephrologists can assist with assessment and treatment. Urologists can determine the need for stone removal.

FEEDING INTOLERANCE

Feeding intolerance can be viewed as the inability to tolerate a calculated "required" volume of nutrition and fluids. It occurs in children who have SNI, for the reasons previously discussed: pain, retching, and vomiting that limit the child's ability to tolerate tube feedings. Feeding intolerance can be a significant source of distress for families, when these symptoms limit the amount of formula that a child can tolerate. Management of this problem includes the interventions summarized in table 5.7.

Most children who have SNI and feeding intolerance have some improvement with these interventions, though not all have the improvement hoped for. Many have significant improvement, some have improvement that is less than desired, and some have a return of symptoms. Returning symptoms may reflect further changes in the areas of the CNS responsible for regulating intestinal motility and vomiting. A child may then experience an escalation of symptoms due to problems such as autonomic dysfunction, visceral hyperalgesia, and central neuropathic pain.

At such times, some children benefit from a 25% to 30% or greater decrease in the total amount of nutrition and fluids provided by a feeding tube. It can be beneficial to define or review the goals of care and set up

plans that meet these goals. This may include feeding to comfort rather than feeding to a "required" amount, as well as withholding feedings that are resulting in significant pain.

"Required" fluids and nutrition

It is useful to review the total volume of nutrition and fluids given each day, including all water flushes. This review starts with an understanding of how fluid and nutrition "requirements" are estimated. Such calculations may overestimate what is needed for some children.

Daily fluid requirement can be estimated by several methods, most commonly by using a child's weight. The estimate is based on the average water losses through urine, stool, evaporation from the skin, and metabolic (energy) expenditure. The fluid requirements can differ if there are deviations from a typical baseline requirement. Conditions that can increase fluid requirements include fever and excessive sweating, as occasionally seen in children with autonomic dysfunction. Conditions that can decrease fluid requirements include decreased metabolic rate, hypothermia, humidified air (as is used for a tracheostomy), and the syndrome of inappropriate antidiuretic hormone (SIADH). As an example, the calculated water requirement should be decreased by 10% to 25% for a low metabolic rate, which is common in children who have SNI. A second method for calculating fluid requirements uses calories expended, calculating 100 to 150 mL of water required per 100 kcal expended. The goal is to provide sufficient water to ensure adequate urine output and to avoid constipation, yet to avoid excessive volume that can contribute to GI symptoms, feeding intolerance, and excessive secretions.

As this information shows, a child with limited activity may not "require" the amount of fluid generally calculated. In addition, a child who has SNI may be more comfortable with a "restriction" in the amount of total fluids; he or she may have less GI pain or feeding intolerance if a smaller volume is given by a feeding tube, with a resulting decrease in visceral distension. A smaller volume of fluid may also help decrease oral secretions.

Parents may feel distressed when considering such decreases in fluids and nutrition. It may be helpful if they consider other medical situations in which fluids are safely restricted, such as for children with congestive heart failure. Parents' fear of dehydration may also be decreased by an understanding that dehydration occurs only when fluid loss exceeds what can be given, typically because of persistent vomiting and diarrhea.

Ben is a 6-year-old boy who has SNI and is fed by a G tube. He is described as "so much more comfortable" after the daily amount of water is dropped from 1,000 mL to 500 mL, yet the parents feel that it took a "standoff" to get agreement from the dietician and medical specialists. This change is a decrease by 30% of his total fluid intake. He continues on the same amount of formula, along with water flushes following medications.

Children with SNI who receive nutrition by a feeding tube are also at risk for excessive weight gain, if the weight-for-length percentile (or body mass index, BMI) is not closely followed. A goal of 50% is not required for these children. Children who are dependent on others for transfers can benefit from a weight-to-length goal of 10% to 25%. This can be accomplished by restricting calorie intake by reducing the volume of formula. Micronutrients (multivitamin, calcium, and phosphorus) and protein can be supplemented as needed.

For some children who have SNI, energy requirements (calories) are even lower than the recommendations for nonambulatory children with cerebral palsy. Risk factors for excessive weight gain in children who have SNI include hypothermia, limited spontaneous movement of the extremities, and the use of an intrathecal baclofen pump (discussed in greater detail in chapter 8). Along with avoiding unnecessary weight gain, a decrease in feedings may minimize "overfeeding" and overdistension as a source of discomfort and feeding intolerance.

Grace has leukoencephalopathy of unknown etiology with associated hypotonia and intellectual disability. She is nonverbal, nonambulatory, and fed by G tube. She enjoys the many family activities in which she participates.

Grace develops increasing vomiting and associated respiratory symptoms when she is 5½ years old. After reviewing contributing factors and intervention options, her team creates a plan that includes decreasing G-tube feeding volume by 35%, with a decrease in formula. She is noted to be more comfortable and less puffy, with elimination of vomiting and improvement in respiratory symptoms. Her next 4 weeks are described as the best she has experienced in months.

When symptoms and feeding intolerance persist

Persistent inability to tolerate nutrition fed directly into the GI tract, whether by G tube or J tube, is an immensely stressful experience for the

families of children who have SNI, as well as for the healthcare teams. It may seem inconceivable that the cause of the problem cannot be found or that interventions cannot improve the problem. For some children, this intolerance can occur after they have tolerated tube feedings for years without difficulty or associated distress. The problem is not considered persistent until the various possible causes and interventions have been considered, as outlined above. The review of problems and interventions typically reflects months of repeated studies, as well as trial and error with various medications and formulas and a J-tube trial. Though this problem is not common, the inherent challenges deserve a comprehensive review.

Tanya, a 9-year-old girl who has cerebral palsy and cognitive impairment resulting from meningitis as an infant, develops G-tube feeding intolerance that has progressed over the previous year to daily vomiting and retching for the past 6 months. Evaluation has been unremarkable, and intervention trials have had no benefit, including multiple blood tests; multiple abdominal X-rays and upper gastrointestinal (UGI) series; upper endoscopy; gastric-emptying studies; treatment for constipation and GER; formula changes; trial with J-tube feedings; and trials with ondansetron and prochlorperazine (Compazine). There have been no other health issues, including no significant respiratory illnesses.

Travis is a 3-year-old who has hydranencephaly with resulting cerebral palsy, cognitive impairment, visual impairment, and seizure disorder. He eats orally, with supplementation of nutrition and fluids by G tube. He is responsive to his family with smiles and laughter. He has remained at his baseline health status until, 3 months ago, he developed vomiting and retching. Symptoms persist despite treatment for constipation and GER, medication trials that include cyproheptadine, erythromycin, and metoclopramide, and a trial of J-tube feedings. He is being considered for Nissen fundoplication surgery.

Why some children who have SNI may develop feeding intolerance

The best we can do is speculate as to why feeding intolerance remains persistent in some children who have SNI or, more typically, abates for a period and then returns, as happened with Tanya. The intolerance may reflect alterations in the CNS, including the areas responsible for motility of the intestinal tract and stimulation of vomiting. Some changes that are linked to CNS function suggest such decline:

- Increasing episodes of low body temperature, low heart rate, and increased sleeping
- Alterations in the autonomic nervous system, with further slowing of intestinal motility
- Increasing retching and pain localized to the GI tract, reflecting an escalation of symptoms from central neuropathic pain and visceral hyperalgesia

It is beneficial at such times to consider "reversible" sources of problems, while simultaneously being mindful that this may be part of a slow, progressive, irreversible decline. This approach can be challenging in caring for children who have SNI, who often experience decline over a long period, increasing the likelihood of "aggressive" evaluation and treatment of an irreversible problem. It is helpful to recognize that even children with "static" neurological conditions probably experience irreversible decline in the CNS, possibly as a result of ongoing neuronal apoptosis (cell death). General anesthesia is another potential risk factor for neuronal cell death, though this hypothesis is based mostly on animal models, including nonhuman primates (Loepke 2010; Rappaport et al. 2011). Decline in the CNS may account for why some children who have SNI develop feeding intolerance later in life that is not amenable to medical interventions (Siden et al. 2009).

This is also a time to recognize and remember the years of benefit that were provided by the feeding tube, even as development of harm from this intervention is considered. It is beneficial to revisit the goals of care, yet not feel obligated to make any decisions. The role of feeding tubes can be viewed as a life-sustaining technology, in the same sense as a ventilator. This allows one to consider the amount of benefit and harm when technology is becoming more burdensome, even when that technology is seen as "routine" and "easy" to use.

The process of considering TPN as an alternative means of providing medical nutrition and hydration can be approached in several ways. First and foremost, it is helpful to consider such technology in the context of how a child is doing overall. A family may view such technology as burdensome and as prolonging suffering, when a child has experienced a decline in other areas of health and function. This decline may be noted as changes in the level of alertness, ability to regulate body temperature and heart rate, frequency of seizures, altered respiratory pattern, overall respiratory health, and level of comfort.

Also helpful is a consideration of what goal is intended by an intervention. Examples of goals are to improve comfort, to restore health, or to maintain life. In the case of Travis, TPN was initiated to improve comfort and feeding tolerance, if possible, as assessed after a time-limited trial. Tanya's parents felt that the potential burden of prolonging suffering offset any consideration of a trial of TPN. Given the months of prior suffering, they felt they could not potentially allow their daughter to experience more suffering.

Discontinuing medical nutrition and hydration remains challenging and controversial, because of the symbolic significance of nutrition, the myths about dehydration and "starvation," and an under-recognition of the complications of artificial hydration and nutrition (Casarett, Kapo, and Caplan 2005). It is ethically permissible to discontinue medical nutrition and hydration when they are identified as prolonging or contributing to suffering (Casarett, Kapo, and Caplan 2005; Diekema and Botkin 2009; Nelson et al. 1995; RCPCH 2004; Stanley 2000). This subject is covered in greater detail in chapters 9 and 10.

Along with the daily retching and vomiting, Tanya has crying spells that range from 2 hours to most of the day, with duration of crying averaging 60% of the day. She is described as "suffering for over 6 months, currently suffering every day." She used to be "very social but now [is] unable to enjoy the activities she did before." The potential role of visceral hyperalgesia and central neuropathic pain are discussed by the team in detail. A symptom care plan includes an increased gabapentin dose (already being used for seizure management), starting cyproheptadine and prn morphine sulfate at a dose of 0.3 mg/kg sublingually, as often as every 1 hour, and decreasing G-tube formula feedings by 25%.

The primary focus of the discussion is Tanya's comfort and the hope for improvement with these interventions. The concept of the G tube as a life-sustaining technology is introduced, with acknowledgment that it is permissible to discontinue any technology that is prolonging suffering. This information is discussed with Tanya's family as an opportunity to inform without any need for a decision.

Tanya has "significant improvement" within 5 days of the new treatment plan, and she is described as being "the best she has looked in the past year." There is a significant reduction in crying spells, vomiting, and retching, and an increase in energy and interaction with her family. She is significantly more comfortable, though not back to her prior baseline. Her parents are delighted;

they hope for continued benefit but are also prepared for a return of symptoms.

Tanya has a return of vomiting, retching, and significant pain 2 months later. "She is suffering every day and unable to enjoy the things she used to enjoy." Her parents cannot imagine allowing her suffering to continue but are also distressed at the thought of discontinuing tube feedings. Follow-up with the palliative care team includes a child life specialist who is developing a supportive plan for Tanya's sisters. Further adjustments in Tanya's medications are made and ongoing follow-up is arranged, including arrangements for home hospice. This plan provides Tanya's parents with the time and support they need as they explore various options. As Tanya's suffering continues despite adjustments to the care plan, a decision is made to discontinue medical nutrition and hydration. Tanya dies 8 days later, with ongoing attention to symptom management and family support.

Travis is hospitalized following an apparent life-threatening event related to an episode of vomiting. A palliative care consultation is initiated. Travis's vomiting and retching continue despite J-tube feedings and venting of the gastrostomy port. Various medication trials include cyproheptadine, with some limited benefit. Erythromycin and metoclopramide are tried, without improvement and with an associated increase in seizures with metoclopramide. Other treatment includes an H-2 blocker, later switched to a PPI, and management of constipation with polyethylene glycol, bisacodyl suppository, and enemas as needed.

Decline in nutrition is assessed as another contributing factor, and TPN is initiated. Home TPN is arranged, with plans to reinitiate J-tube feeding at home, but attempts to reinitiate tube feedings fail. Travis is later admitted to the hospital with a fever and positive blood culture resulting from a line infection. The palliative care team again meets with the parents to establish goals of care and identify symptom management strategies. The team notes that Travis is uncomfortable more than half of each day. He is described as "struggling," "fighting to stay alive," "uncomfortable," and needing to be held and repositioned often to be comfortable. This situation is in contrast to 6 months ago, when the majority of his days were enjoyable and comfortable. His parents feel they have "lost" part of Travis but continue to hope for improvement in functional and health status. No improvement occurs, despite treatment of the line infection, placement of a new line, and continued TPN. The discussion recognizes the role of TPN as a life-sustaining medical treatment to be continued as long as it is meeting identified goals. Home TPN and home hos-

pice are arranged, with support to "hope for the best" while "preparing for the rest."

Once Travis is home, minimal J-tube feedings are introduced several times, resulting in discomfort, abdominal distension, and vomiting. The follow-up discussion includes the low likelihood of bridging back to tube feedings and the risk with continued TPN. Travis is observed to develop peripheral edema (swelling of body tissue, noted in the arms, legs, and face) with his current "maintenance" volume of fluids, assessed as a decline in the body's ability to process the nutrition and fluid given intravenously. A decision is made to discontinue medical nutrition and hydration and to use interventions for comfort. Travis dies peacefully at home in his mother's arms, with his family feeling prepared and supported.

It is important to note that the parents in these cases did not indicate distress or discomfort over these discussions. Instead, they were distressed at seeing their child's persistent suffering and feeling helpless and hopeless about it. It is common to observe a family's simultaneous relief and grief over the thought that "my hope for my child's comfort can be realized, but it will be at the cost of losing my child." In the broadest sense, this again reflects how families often hope and prepare, how hope is always possible, but how what is hoped for may shift over time from preserving health and comfort to preserving comfort. These challenges and themes are revisited in chapter 9.

TAKE-HOME POINTS

- Evaluation and treatment of gastroesophageal reflux disease is summarized in tables 5.2 and 5.3.
- Metoclopramide must be used cautiously, because it can result in dystonia, seizures, and irritability.
- Persistent vomiting that is associated with retching and discomfort is probably due to causes beyond GERD.
- GERD can coexist with the other sources of persistent vomiting and retching.
- Sources of persistent vomiting and retching in children with impairment of the central nervous system include autonomic dysfunction, stimulation of the vomiting reflex, and visceral hyperalgesia.
- Tables 5.1 and 5.7 summarize the sources and treatment of retching and vomiting.

- Individuals with recurrent hypothermia due to impairment in the ability of the CNS to regulate body temperature are at risk for pancreatitis (inflammation of the pancreas).
- Diarrhea can occur as a result of liquid medications in a sorbitol base, frequent antibiotic use, *Clostridium difficile* (C. diff), magnesium-containing antacids, and small bowel bacterial overgrowth.
- Slow motility of the intestinal tract can result in small bowel bacterial overgrowth, with symptoms of excessive gas, distension of the abdomen, abdominal pain, and chronic diarrhea.
- Retention of urine in the bladder can increase the risk for urinary tract (bladder) infection.
- Constipation can cause or contribute to urinary retention and bladder infection.
- Renal (kidney) stones occur at a higher rate in children on the ketogenic diet or taking zonisamide or topiramate; calcium and vitamin D supplementation may also contribute by increasing urinary excretion of calcium.
- Nonambulatory children treated with topiramate may have an even greater risk for renal stones compared with the general population.
- The amount of nutrition and fluids given should be reviewed so as to avoid overfeeding, which can cause discomfort and excessive weight gain.
- Retching, vomiting, and associated pain can become intractable in some children.

References

Abell TL, Adams KA, Boles RG, et al. 2008. Cyclic vomiting syndrome in adults. *Neurogastroenterol Motil* 20(4):269–84.

Antao B, Ooi K, Ade-Ajayi N, et al. 2005. Effectiveness of alimemazine in controlling retching after Nissen fundoplication. *J Pediatr Surg* 40(11):1737–40.

Antonarakis ES, Hain RD. 2004. Nausea and vomiting associated with cancer chemotherapy: drug management in theory and in practice. *Arch Dis Child* 89(9):877–80.

Axelrod FB, Berlin D. 2009. Pregabalin: a new approach to treatment of the dysautonomic crisis. *Pediatrics* 124(2):743–46.

Baguley IJ, Cameron ID, Green AM, et al. 2004. Pharmacological management of dysautonomia following traumatic brain injury. *Brain Inj* 18(5):409–17.

Baguley IJ, Heriseanu RE, Gurka JA, et al. 2007. Gabapentin in the management of dysautonomia following severe traumatic brain injury: a case series. *J Neurol Neurosurg Psychiatry* 78(5):539–41.

Böhmer CJ, Klinkenberg-Knol EC, Niezen-de Boer MC, Meuwissen SG. 2000. Gastroesophageal reflux disease in intellectually disabled individuals: how often, how serious, how manageable? *Am J Gastroenterol* 95(8):1868–72.

Bui HD, Dang CV, Chaney RH, Vergara LM. 1989. Does gastrostomy and fundoplication prevent aspiration pneumonia in mentally retarded persons? *Am J Ment Retard* 94(1): 16–19.

Burrati S, Kamenwa R, Dohil R, et al. 2004. Esophagogastric disconnection following failed fundoplication for the treatment of gastroesophageal reflux disease (GERD) in children with severe neurological impairment. *Pediatr Surg Int* 20(10):786–90.

Bustorff-Silva J, Fonkalsrud EW, Perez CA, et al. 1999. Gastric emptying procedures decrease the risk of postoperative recurrent reflux in children with delayed gastric emptying. *J Pediatr Surg* 34(1):79–82; discussion 82–83.

Casarett D, Kapo J, Caplan A. 2005. Appropriate use of artificial nutrition and hydration—fundamental principles and recommendations. *N Engl J Med* 353(24):2607–12.

Chelimsky G, Chelimsky T. 2001. Familial association of autonomic and gastrointestinal symptoms. *Clin Auton Res* 11(6):383–86.

Chelimsky G, Hupertz VF, Chelimsky TC. 1999. Abdominal pain as the presenting symptom of autonomic dysfunction in a child. *Clin Pediatr (Phila)* 38(12):725–29.

Cheung KM, Tse PW, Ko CH, et al. 2001. Clinical efficacy of proton pump inhibitor therapy in neurologically impaired children with gastroesophageal reflux: prospective study. *Hong Kong Med J* 7(4):356–59.

Cheung KM, Tse HW, Tse PW, Chan KH. 2006. Nissen fundoplication and gastrostomy in severely neurologically impaired children with gastroesophageal reflux. *Hong Kong Med J* 12(4):282–88.

Chicella MF, Batres LA, Heesters MS, Dice JE. 2005. Prokinetic drug therapy in children: a review of current options. *Ann Pharmacother* 39(4):706–11.

Complex Child E-Magazine. 2009. Neuro-crying, neuro-irritability, or pain? A personal account. www.articles.complexchild.com/nov2009/00166.html.

Conway PH, Cnaan A, Zaoutis T, et al. 2007. Recurrent urinary tract infections in children: risk factors and association with prophylactic antimicrobials. *JAMA* 298(2):179–86.

Curran MP, Robinson DM. 2009. Aprepitant: a review of its use in the prevention of nausea and vomiting. *Drugs* 69(13):1853–78.

Curry JI, Lander TD, Stringer MD. 2001. Review article: erythromycin as a prokinetic agent in infants and children. *Aliment Pharmacol Ther* 15(5):595–603.

Danielson PD, Emmens RW. 1999. Esophagogastric disconnection for gastroesophageal reflux in children with severe neurological impairment. *J Pediatr Surg* 34(1):84–87.

Daudon M, Jungers P. 2004. Drug-induced renal calculi: epidemiology, prevention and management. *Drugs* 64(3):245–75.

Delgado-Aros S, Camilleri M. 2003. Pseudo-obstruction in the critically ill. *Best Pract Res Clin Gastroenterol* 17(3):427–44.

Delgado-Aros S, Camilleri M. 2005. Visceral hypersensitivity. *J Clin Gastroenterol* 39(Suppl 3):S194–203.

Del Giudice E, Staiano A, Capano G, et al. 1999. Gastrointestinal manifestations in children with cerebral palsy. *Brain Dev* 21(5):307–11.

de Veer AJ, Bos JT, Niezen-de Boer RC, et al. 2008. Symptoms of gastroesophageal reflux disease in severely mentally retarded people: a systematic review. *BMC Gastroenterol* 8:23.

Diekema DS, Botkin JR, Committee on Bioethics. 2009. Clinical report: forgoing medically provided nutrition and hydration in children. *Pediatrics* 124(2):813–22.

Dunn JC, Lai EC, Webber MM, et al. 1998. Long-term quantitative results following fundoplication and antroplasty for gastroesophageal reflux and delayed gastric emptying in children. *Am J Surg* 175(1):27–29.

Edes TE, Walk BE, Austin JL. 1990. Diarrhea in tube-fed patients: feeding formula not necessarily the cause. *Am J Med* 88(2):91–93.

Emmanuel AV, Shand AG, Kamm MA. 2004. Erythromycin for the treatment of chronic intestinal pseudo-obstruction: description of six cases with a positive response. *Aliment Pharmacol Ther* 19(6):687–94.

Feldstein TJ. 1996. Carbohydrate and alcohol content of 200 oral liquid medications for use in patients receiving ketogenic diets. *Pediatrics* 97(4):506–11.

Friedman JN, Ahmed S, Connolly B, et al. 2004. Complications associated with image-guided gastrostomy and gastrojejunostomy tubes in children. *Pediatrics* 114(2):458–61.

Gan TJ, Apfel CC, Kovac A, et al., Aprepitant-PONV Study Group. 2007. A randomized, double-blind comparison of the NK1 antagonist, aprepitant, versus ondansetron for the prevention of postoperative nausea and vomiting. *Anesth Analg* 104(5):1082–89.

Gilles EE. 2011. "Neuro-irritability" in children with developmental disabilities: the role of autonomic nervous system dysregulation. *Neuropädiatrie* 10(1):15–19.

Gillette MA, Knott A, Frohnapple DJ. 2011. Case report: use of a new delayed release pancrelipase formulation to clear obstructed feeding tubes. *Hosp Pharm* 46(4):269–72.

Gmora S, Poenaru D, Tsai E. 2002. Neostigmine for the treatment of pediatric acute colonic pseudo-obstruction. *J Pediatr Surg* 37(10):E28.

Gore L, Chawla S, Petrilli A, et al., Adolescent Aprepitant in Cancer Study Group. 2009. Aprepitant in adolescent patients for prevention of chemotherapy-induced nausea and vomiting: a randomized, double-blind, placebo-controlled study of efficacy and tolerability. *Pediatr Blood Cancer* 52(2):242–47.

Goulet O, Jobert-Giraud A, Michel JL, et al. 1999. Chronic intestinal pseudo-obstruction syndrome in pediatric patients. *Eur J Pediatr Surg* 9(2):83–89.

Goyal M, Grossberg RI, O'Riordan MA, Davis ID. 2009. Urolithiasis with topiramate in nonambulatory children and young adults. *Pediatr Neurol* 40(4):289–94.

Grotenhermen F. 2005. Cannabinoids. *Curr Drug Targets CNS Neurol Disord.* 4(5):507–30.

Hament JM, Bax NM, van der Zee DC, et al. 2001. Complications of percutaneous endoscopic gastrostomy with or without concomitant antireflux surgery in 96 children. *J Pediatr Surg* 36(9):1412–15.

Hasler ML. 2003. Pharmacotherapy for intestinal motor and sensory disorders. *Gastroenterol Clin North Am* 32(2):707–32.

Hauer JM. 2008. Central hypothermia as a cause of acute pancreatitis in children with neurodevelopmental impairment. *Dev Med Child Neurol* 50(1):68–70.

Heimburger DC, Sockwell DG, Geels WJ. 1994. Diarrhea with enteral feeding: prospective reappraisal of putative causes. *Nutrition* 10(5):392–96.

Heneyke S, Smith VV, Spitz L, Milla PJ. 1999. Chronic intestinal pseudo-obstruction: treatment and long term follow up of 44 patients. *Arch Dis Child* 81(1):21–27.

Hibbs AM, Lorch SA. 2006. Metoclopramide for the treatment of gastroesophageal reflux disease in infants: a systematic review. *Pediatrics* 118(2):746–52.

Houghton LA, Fell C, Whorwell PJ, et al. 2007. Effect of a second-generation alpha2delta ligand (pregabalin) on visceral sensation in hypersensitive patients with irritable bowel syndrome. *Gut* 56(9):1218–25.

Jancar J, Speller CJ. 1994. Fatal intestinal obstruction in the mentally handicapped. *J Intellect Disabil Res* 38(Pt 4):413–22.

Jiang DP, Li ZZ, Guan SY, Zang YB. 2007. Treatment of pediatric Ogilvie's syndrome with low-dose erythromycin: a case report. *World J Gastroenterol* 13(13):2002–3.

Kawahara H, Okuyama H, Kubota A, et al. 2004. Can laparoscopic antireflux surgery improve the quality of life in children with neurologic and neuromuscular handicaps? *J Pediatr Surg* 39(12):1761–64.

Khajanchee YS, Dunst CM, Swanstrom LL. 2009. Outcomes of Nissen fundoplication in patients with gastroesophageal reflux disease and delayed gastric emptying. *Arch Surg* 144(9):823–28.

Kloos RT. 1995. Spontaneous periodic hypothermia. *Medicine (Baltimore)* 74(5):268–80.

Koletzko S, Jones NL, Goodman KJ, et al., H pylori Working Groups of ESPGHAN and NASPGHAN. 2011. Evidence-based guidelines from ESPGHAN and NASPGHAN for *Helicobacter pylori* infection in children. *J Pediatr Gastroenterol Nutr* 53(2):230–43.

Kumpf V. 2012. Evaluation of a protocol for restoring patency of enteral feeding tubes. American Society of Parenteral and Enteral Nutrition. Clinical Nutrition Week posters.

Lee KJ, Kim JH, Cho SW. 2005. Gabapentin reduces rectal mechanosensitivity and increases rectal compliance in patients with diarrhoea-predominant irritable bowel syndrome. *Aliment Pharmacol Ther* 22(10):981–88.

Lee SL, Shabatian H, Hsu JW, et al. 2008. Hospital admissions for respiratory symptoms and failure to thrive before and after Nissen fundoplication. *J Pediatr Surg* 43(1):59–63; discussion 63–65.

Loepke AW. 2010. Developmental neurotoxicity of sedatives and anesthetics: a concern for neonatal and pediatric critical care medicine? *Pediatr Crit Care Med* 11(2):217–26.

Lord LM. 2003. Restoring and maintaining patency of enteral feeding tubes. *Nutr Clin Pract* 18(5):422–26.

McKay CP. 2010. Renal stone disease. *Pediatr Rev* 31(5):179–88.

Mousa H, Caniano DA, Alhajj M, et al. 2006. Effect of Nissen fundoplication on gastric motor and sensory functions. *J Pediatr Gastroenterol Nutr* 43(2):185–89.

Nelson LJ, Rushton CH, Cranford RE, et al. 1995. Forgoing medically provided nutrition and hydration in pediatric patients. *J Law Med Ethics* 23(1):33–46.

O'Dea CJ, Brookes JH, Wattchow DA. 2010. The efficacy of treatment of patients with severe constipation or recurrent pseudo-obstruction with pyridostigmine. *Colorectal Dis* 12(6):540–48.

Ponec RJ, Saunders MD, Kimmey MB. 1999. Neostigmine for the treatment of acute colonic pseudo-obstruction. *N Engl J Med* 341(3):137–41.

Proujansky R, Shaffer SE, Vinton NE, Bachrach SJ. 1994. Symptomatic *Helicobacter pylori* infection in young patients with severe neurologic impairment. *J Pediatr* 125(5 Pt 1): 750–52.

Quigley EM, Abu-Shanab A. 2010. Small intestinal bacterial overgrowth. *Infect Dis Clin North Am* 24(4):943–59.

Rappaport B, Mellon RD, Simone A, Woodcock J. 2011. Defining safe use of anesthesia in children. *N Engl J Med* 364(15):1387–90.

RCPCH (Royal College of Paediatrics and Child Health). 2004. Withholding or withdrawing life sustaining treatment for children: a framework for practice. www.rcpch.ac.uk/what-we-do/rcpch-publications/publications-list-title/publications-list-title.

Richards CA, Andrews PL, Spitz L, Milla PJ. 1998. Nissen fundoplication may induce gastric myoelectrical disturbance in children. *J Pediatr Surg* 33(12):1801–5.

Richards CA, Milla PJ, Andrews PL, Spitz L. 2001. Retching and vomiting in neurologically impaired children after fundoplication: predictive preoperative factors. *J Pediatr Surg* 36(9):1401–4.

Rubiales AS, Hernansanz S, Gutiérrez C, et al. 2006. Neostigmine for refractory constipation in advanced cancer patients. *J Pain Symptom Manage* 32(3):204–5.

Ruiz C, Gener B, Garaizar C, Prats JM. 2003. Episodic spontaneous hypothermia: a periodic childhood syndrome. *Pediatr Neurol* 28(4):304–6.

Schwarz SM, Corredor J, Fisher-Medina J, et al. 2001. Diagnosis and treatment of feeding disorders in children with developmental disabilities. *Pediatrics* 108(3):671–76.

Sheen E, Triadafilopoulos G. 2011. Adverse effects of long-term proton pump inhibitor therapy. *Dig Dis Sci* 56(4):931–50.

Sherman PM, Hassall E, Fagundes-Neto U, et al. 2009. A global, evidence-based consensus on the definition of gastroesophageal reflux disease in the pediatric population. *Am J Gastroenterol* 104(5):1278–95.

Sheth RD, Barron TF, Hartlage PL. 1994. Episodic spontaneous hypothermia with hyperhidrosis: implications for pathogenesis. *Pediatr Neurol* 10(1):58–60.

Siden H, Tucker T, Derman S, et al. 2009. Pediatric enteral feeding intolerance: a new prognosticator for children with life-limiting illness? *J Palliat Care* 25(3):213–17.

Smith RM, Myers SA. 2005. 2 devices that unclog feeding tubes. *RN* 68(1):36–41.

Spiroglou K, Xinias I, Karatzas N, et al. 2004. Gastric emptying in children with cerebral palsy and gastroesophageal reflux. *Pediatr Neurol* 31(3):177–82.

Srivastava R, Berry JG, Hall M, et al. 2009. Reflux related hospital admissions after fundoplication in children with neurological impairment: retrospective cohort study. *BMJ* 339:b4411.

Srivastava R, Downey EC, O'Gorman M, et al. 2009. Impact of fundoplication versus gastrojejunal feeding tubes on mortality and in preventing aspiration pneumonia in young children with neurologic impairment who have gastroesophageal reflux disease. *Pediatrics* 123(1):338–45.

Stanley AL. 2000. Withholding artificially provided nutrition and hydration from disabled children—assessing their quality of life. *Clin Pediatr (Phila)* 39(10):575–79.

Steinherz R, Levy Y, Ban-Amiti D, et al. 1986. Extrapyramidal reactions to domperidone. *J Pediatr* 108(4):630–31.

Struijs MC, Lasko D, Somme S, Chiu P. 2010. Gastric emptying scans: unnecessary preoperative testing for fundoplications? *J Pediatr Surg* 45(2):350–54.

Subramaniam R, Dickson AP. 2000. Long-term outcome of Boix-Ochoa and Nissen fundoplication in normal and neurologically impaired children. *J Pediatr Surg* 35(8): 1214–16.

Sullivan PB. 2008. Gastrointestinal disorders in children with neurodevelopmental disabilities. *Dev Disabil Res Rev* 14(2):128–36.

Tonini M, Cipollina L, Poluzzi E, et al. 2004. Review article: clinical implications of enteric and central D2 receptor blockade by antidopaminergic gastrointestinal prokinetics. *Aliment Pharmacol Ther* 19(4):379–90.

Vandenplas Y, Rudolph CD, Di Lorenzo C, et al. 2009. Pediatric gastroesophageal reflux clinical practice guidelines: joint recommendations of the North American Society

for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN). *J Pediatr Gastroenterol Nutr* 49(4):498–547.

Wales PW, Diamond IR, Dutta S, et al. 2002. Fundoplication and gastrostomy versus image-guided gastrojejunal tube for enteral feeding in neurologically impaired children with gastroesophageal reflux. *J Pediatr Surg* 37(3):407–12.

Zangen T, Ciarla C, Zangen S, et al. 2003. Gastrointestinal motility and sensory abnormalities may contribute to food refusal in medically fragile toddlers. *J Pediatr Gastroenterol Nutr* 37(3):287–93.

CHAPTER 6

Respiratory Problems

Pneumonia, Excessive Secretions, and Respiratory Distress

Worry does not empty tomorrow of its sorrow.
It empties today of its strength.
—Corrie Ten Boom

Respiratory problems are the most common cause of illness in children and adults with severe neurological impairment. They are also a great source of distress for children and their families, creating worries about the life-threatening risk associated with recurrent respiratory illness, the decision to use mechanical support of breathing, and the physical distress that can accompany each respiratory illness. Information cannot eliminate these worries, but a comprehensive review of care plans that can both maximize health and address respiratory distress can empower parents before more difficult decisions are encountered.

WHY CHILDREN WHO HAVE SNI DEVELOP RESPIRATORY PROBLEMS

The job of the respiratory system is to exchange oxygen (O_2) and carbon dioxide (CO_2) between the air we breathe and the blood vessels in our bodies. Oxygen from the air is delivered to the lungs, exchanged into the blood, and then delivered throughout the body. Ridding the body of the carbon dioxide produced in the cells is the reverse of this process. The goal of this system is to maintain the body's oxygen and carbon dioxide at levels that sustain the health and functioning of all cells in the body.

This process involves the mechanics of the muscles that expand and contract the lungs, referred to as the respiratory muscles; the areas of the brain that transmit nerve impulses to these muscles, referred to as the

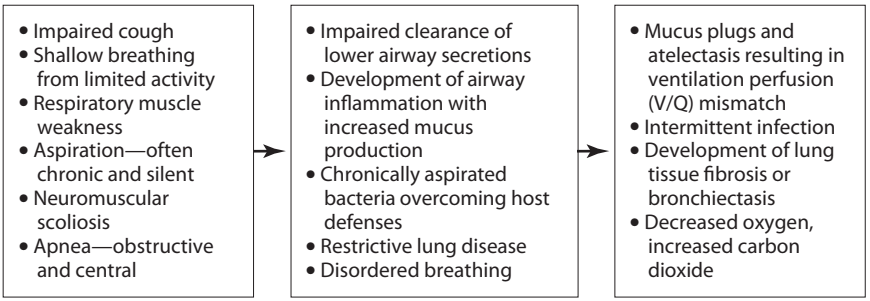

• Impaired cough
• Shallow breathing from limited activity
• Respiratory muscle weakness
• Aspiration—often chronic and silent
• Neuromuscular scoliosis
• Apnea—obstructive and central
• Impaired clearance of lower airway secretions
• Development of airway inflammation with increased mucus production
• Chronically aspirated bacteria overcoming host defenses
• Restrictive lung disease
• Disordered breathing
• Mucus plugs and atelectasis resulting in ventilation perfusion (V/Q) mismatch
• Intermittent infection
• Development of lung tissue fibrosis or bronchiectasis
• Decreased oxygen, increased carbon dioxide

Figure 6.1. Sources of respiratory problems

respiratory centers; and the diffusion of oxygen and carbon dioxide between the lung tissue and the blood vessels that surround the air sacs, the final branches of the lungs, where gas exchange takes place. Impairment in any part of the respiratory system will alter the body's ability to provide adequate oxygen to the cells and expel carbon dioxide from the body.

Children who have SNI are at risk for a number of problems that can impair the job of the respiratory system (figure 6.1). Abnormal motor control and tone can alter the ability to expel mucus from the lungs and to keep the lungs adequately expanded. Impaired motor coordination can result in a swallowing dysfunction and chronic microaspiration of secretions from the mouth. These problems can then contribute to chronic inflammation and infection, with the subsequent risk of developing fibrosis and impairment of gas exchange. In addition, impairment in the areas of the central nervous system that control ventilation can result in disordered breathing and central apnea. Other factors to consider include neuromuscular (NM) scoliosis, obstructive apnea, and gastroesophageal reflux (GER). Treatment can involve interventions that assist with the clearance of mucus and secretions in the lungs, minimize the development of inflammation, and treat infection and inflammation at times of acute respiratory illness.

Atelectasis, mucus plugs, and ventilation perfusion mismatch

Atelectasis is the collapse of the lung's air sacs (alveoli), resulting in reduced or absent gas exchange within the air sacs. In children who have SNI, atelectasis is most commonly a result of mucus in the smaller airways of the lungs. Mucus can cause a blockage of airflow in the lungs, called a mucus plug, with collapse of the lung tissue distal to the area of the blockage. Children with SNI have an increased risk of developing atelectasis, for

several reasons (listed in the first two panels of figure 6.1). These include impaired mucus mobilization from the lungs and increased mucus production due to inflammation resulting from chronic microaspiration.

Ventilation perfusion (V/Q) mismatch is a consequence of atelectasis. A V/Q mismatch is a mismatch, or imbalance, in the areas of the lung available for gas exchange with the capillaries (smallest blood vessels). Hemoglobin in the capillaries normally picks up oxygen from the air sacs of the lungs. The capillaries deliver this oxygenated blood to the large blood vessels that empty into the heart, and the oxygen is then delivered through the blood vessels from the heart to the body. In atelectasis, the capillaries where the air sacs are collapsed cannot pick up oxygen. The blood containing less oxygen from these capillaries then mixes with the blood from other areas of the lung. As a result, overall, the mixture of blood leaving the lungs carries less oxygen.

V/Q mismatch can be noted when an acute collapse of lung tissue caused by a mucus plug results in a sudden decrease in measured oxygen saturation (O_2 sats). Interventions that help clear mucus, such as chest physiotherapy (chest PT), can minimize the development of such plugs and assist acutely with opening the plugged area. When such an intervention helps mobilize a mucus plug, a sudden increase in the oxygen saturation can be observed.

Aspiration, pneumonia, and acute respiratory exacerbations

Aspiration is defined as the passage of foreign material, such as food, gastric content, and saliva, into the airways and lower respiratory tract. Approximately half of all healthy adults aspirate small amounts of oropharyngeal secretions during sleep (Gleeson, Eggli, and Maxwell 1997; Huxley et al. 1978). Mechanisms exist to clear the infectious material without further consequence, including forceful coughing, ciliary transport (cilia are tiny hairs in the airways that sweep mucus and debris out of the lungs), and immune mechanisms that protect against infection. When any of these mechanisms are impaired, as they are in children who have SNI, inflammation and infection can follow.

Aspiration during oral feedings can result in such symptoms as coughing, choking, and gagging. In children without a protective gag reflex or coughing, aspiration can be silent as food and liquid enter the lungs. In addition, chronic aspiration of saliva is commonly silent, probably reflecting a volume that is too small to produce symptoms, as saliva from the mouth intermittently enters the airways and lung. This process is often

referred to as microaspiration. Aspiration can contribute to both inflammation and infection.

When aspiration is suspected, a videofluoroscopic swallow study (VSS) can be obtained. Reasons to consider a VSS include symptoms with feeding, chronic respiratory symptoms, and recurrent respiratory illness. The VSS study can determine whether aspiration occurs with liquids only and whether there is a liquid consistency that does not result in aspiration, such as liquids thickened to nectar, honey, or pudding consistency.

When a child who has SNI develops recurrent respiratory illness, "pneumonia" or "aspiration pneumonia" is commonly used to explain each acute illness. For a parent, such labels can give the impression of an isolated infection or an acute aspiration event. Instead, these acute illnesses should be seen as resulting from the chronic contributing factors indicated earlier. The term *respiratory exacerbation* is frequently used in this chapter in recognition of the many contributing factors that intermittently overcome host defenses and manifest as recurrent respiratory illness (figure 6.2).

This approach to considering respiratory illness is beneficial because it keeps the emphasis on all contributing problems. The goal is to use such information to guide when to initiate acute treatment options, including antibiotics and steroids. Information that suggests secondary infection includes fever and an increase in the amount of coughing, wheezing, and respiratory secretions, despite the use of inhaled medications and interventions to improve clearance of mucus in the lungs. Overall, the goal of chronic and acute treatment is to minimize the effect of contributing factors (figure 6.2) and maximize the maintenance and recovery of health (see figure 6.3). The use of chronic and acute treatment interventions can often maintain the individual's health and comfort over many years.

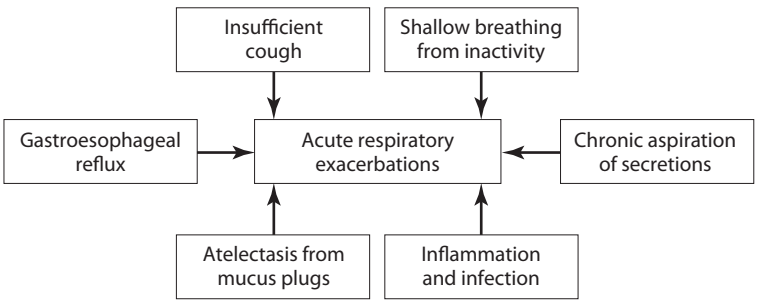


Figure 6.2. Problems that contribute to acute respiratory exacerbations

Finally, inflammation and infection can result in a vicious cycle. The problems that contribute to recurrent respiratory illness in children who have SNI contribute to the development of inflammation and infection, and each contributes to further development of the other: inflammation is the body's response to foreign material such as bacteria, and the mucus that results from inflammation creates an environment that increases the development of mucus plugs and bacterial infection.

Gastroesophageal reflux and reflux aspiration

Aspiration can involve liquids and solids that are swallowed; stomach contents, as a result of gastroesophageal reflux; and saliva from the mouth. GER may contribute to the ill effects of chronic pulmonary aspiration, though its significance remains unclear. Aspiration of contents from the stomach can cause harm partly due to the acid level, with the pH of gastric fluid often ranging between 1.5 and 3.5. This risk can be significant, as pH levels of 1 to 2.5 are considered to be toxic to the lungs (Marik 2001). One study showed that GER without associated aspiration was not a risk factor for the development of lower respiratory tract infections in children with severe neurological disability (Morton, Wheatley, and Minford 1999). The limited benefit of Nissen fundoplication (reviewed in greater detail below; see "Surgical interventions") in decreasing the frequency of lower respiratory tract infections may speak to the limited role of GER in contributing to the ill effects of chronic pulmonary aspiration.

The finding that GER can cause similar respiratory symptoms with or without aspiration challenges the clinical picture (Stein 2003). In addition, it is difficult to distinguish whether vomiting in a child with increased risk for aspiration is the primary *source* of an acute event or is a *result* of increased respiratory symptoms.

In general, then, GER can contribute to respiratory symptoms but should not be considered the sole cause of recurrent respiratory illness in children who have SNI. Rather, it is best viewed as contributing to chronic symptoms and recurrent respiratory exacerbations.

Pulmonary fibrosis and bronchiectasis

Pulmonary fibrosis, the development of scar tissue in the lungs, is one of the complications of chronic aspiration into the lungs (J. S. Lee et al. 2010). This fibrosis can result in decreased oxygen diffusion across the scarred

lung tissue. In addition, the lungs can become stiffer, resulting in restrictive lung disease (discussed below).

Bronchiectasis is a morphological term, indicating abnormal permanent dilation of the bronchi (Eastham et al. 2004; Goeminne and Dupont 2010; Stafler and Carr 2010). Associated problems include reduced clearance of airway mucus, increased mucus production, and dilation, thickening, and destruction of the airway wall, with loss of structural integrity. Children who have SNI are at risk for bronchiectasis as a result of chronic aspiration, and the condition causes further impairment in the ability to clear secretions, as well as increasing the production of pulmonary mucus. Management includes many of the same interventions used both chronically and acutely for children who have SNI and respiratory problems, as described later in the chapter.

Obstructive and central apnea

Children who have SNI are at increased risk for both obstructive apnea and centrally mediated apnea (L. K. Brown 2010; Javaheri 2010; Katz and D'Ambrosio 2010; Katz, McGrath, and Marcus 2000; Marcus 2001). Obstructive sleep apnea occurs when obstruction of the upper airway disrupts the normal airflow during sleep and thus disrupts normal sleep patterns (Katz and D'Ambrosio 2010; Marcus 2001). A sleeping child may snore, have labored breathing, and have episodes of increased respiratory effort associated with lack of airflow and pauses in snoring, followed by gasping or arousal. Children with obstructive apnea are at risk for irritability or excessive daytime sleepiness as a result of disruption in the normal sleep pattern. Problems in children who have SNI that can increase the risk for obstructive apnea include abnormal motor tone and muscle control of the upper airway, inability to reposition themselves during an obstructive event, or congenital syndromes that alter the craniofacial structure of the upper airway.

Pain may contribute to increased muscle tone and thereby worsen obstructive apnea, as illustrated by the case of Sofia described later in the chapter (see "Case examples"). Hypertonia contributing to obstructive apnea is suggested by a case report of a young woman with cerebral palsy whose obstructive apnea resolved following the use of an intrathecal baclofen (ITB) pump (McCarty, Gaebler-Spira, and Harvey 2001). Other potential contributing factors associated with pain and hypertonia that can alter the airway and the muscle coordination of breathing include stiffening,

arching, and posturing. Pain treatment that lessens these problems may improve respiratory function in some (Hauer and Mackey 2012).

In central apnea, the respiratory effort is diminished or absent, intermittently or cyclically. Children who have SNI are at risk for central apnea as a result of impairment in the respiratory centers of the medulla and pons (L. K. Brown 2010; Javaheri 2010; Marcus 2001). Central hypoventilation in children has also been associated with hypothalamic dysfunction and autonomic dysfunction, problems seen in some children who have SNI (Ize-Ludlow el al. 2007; Katz, McGrath, and Marcus 2000).

Restrictive lung disease

Restrictive lung disease is characterized by a reduction in total lung volume. It can be caused by fibrosis with a resulting decrease in lung elasticity or by a problem related to expansion of the chest wall during inhalation. Neuromuscular scoliosis is probably the most common reason for restrictive lung disease in children who have SNI. Pulmonary fibrosis is another possible cause.

Summary of problems that cause altered respiratory health

Table 6.1 summarizes the problems that can alter respiratory health in children who have SNI. In general, the problems reflect impairment of the "mechanics" that are regulated by the CNS (impaired clearance of secretions, shallow and restricted breathing, aspiration, apnea) and the development of intermittent and chronic impairment of gas exchange in the lungs (atelectasis, pneumonia, scarring of lung tissue, bronchiectasis).

Taking an approach that considers the several problems that can contribute to chronic symptoms and recurrent exacerbations reflects the view that the various diagnoses used for respiratory illness often cannot be distinguished: mucus plugs with atelectasis, pneumonia, aspiration pneumonia, vomiting with aspiration, and asthma—all of these have similar symptoms. When vomiting does occur, it is difficult to distinguish vomiting that contributed to an acute respiratory exacerbation from vomiting secondary to increased coughing and respiratory secretions. In children with no oral intake, aspiration is less likely to be a discrete "event" and more likely to represent gradual changes due to silent microaspiration.

Any decline in the health of the lungs, as a result of these contributing problems, generally occurs gradually. Many children experience a decline

TABLE 6.1 Summary of problems that cause altered respiratory health

Problem	What is it?	Why does it happen? Other comments
Atelectasis	• Collapse of lung tissue as a result of blockage in the airways (bronchi or bronchioles) • Commonly caused by a buildup of mucus in the lungs, often referred to as mucus plugs	• Impaired clearance of mucus and secretions from the lungs as a result of less-effective coughing • Inflammation in response to aspiration and impaired mucus clearance • Shallow breathing resulting in decreased expansion of lungs
Ventilation perfusion (V/Q) mismatch	• Mismatch or imbalance in the areas of the lung available for exchange of oxygen and carbon dioxide with blood vessels • As a result, blood leaving the lungs carries less oxygen	• A result of atelectasis and pneumonia • Can lead to a gradual or sudden drop in measured oxygen saturation (O_2 sats), then a sudden increase following interventions that move the mucus forward and open a collapsed area of the lung
Aspiration and pneumonia	• Aspiration: passage of material into the lungs, including swallowed food, content from the stomach as a result of GER, and saliva from the mouth • Pneumonia: inflammation of the lungs, often resulting from infection	• Symptoms and illness from aspiration can be both acute and chronic • "Aspiration pneumonia" in a child who has SNI and recurrent respiratory illness is often a result of the multiple factors indicated in figure 6.2
Gastroesophageal reflux (GER)	• Movement of stomach content across the lower esophageal sphincter into the esophagus	• Symptoms include wheezing, congestion, vomiting, and irritability
Respiratory exacerbation	• In this book, refers to acute respiratory illness that is recurrent in children who have SNI, due to multiple factors	• Contributing factors include impaired clearance of mucus from the lungs, chronic inflammation, and recurrent infection

(continued)

TABLE 6.1 *(continued)*

Problem	What is it?	Why does it happen? Other comments
Lung scarring and bronchiectasis	• Chronic aspiration and inflammation can result in scarring of lung tissue (fibrosis) • Bronchiectasis: abnormal, permanent dilation of the large airways (bronchi)	• Scarring of the lungs can impair the transfer of oxygen between the lungs and blood vessels, which can result in the lungs becoming stiffer and more difficult to expand • Bronchiectasis also contributes to increased mucus production
Obstructive and central apnea	• Apnea: temporary pause or marked reduction in breathing • Obstructive apnea: no air flows into or out of the lungs, despite the effort of breathing • Central apnea: reduced or absent breathing effort	• Obstructive apnea is associated with abnormal motor tone and muscle control of the upper airway, inability to reposition, structural abnormalities, and pain resulting in increased muscle tone of the airway • Central apnea occurs when the brain does not send the proper signal to the muscles that control breathing
Restrictive lung disease	• Reduction in total lung volume	• Scoliosis and lung scarring can contribute to restrictive lung disease

over years, if not decades. This is often noted as an increasing frequency of respiratory exacerbations and decreasing benefit from acute treatment.

SYMPTOMS THAT SUGGEST RESPIRATORY PROBLEMS

The common symptoms observed with respiratory problems are reviewed in table 6.2. Some children are at risk of developing these problems but do not display these symptoms. Such children tend to have the greatest neurological impairment and, as a result, they may have no cough or protective gag reflex. Children with the greatest impairment are also at

TABLE 6.2 Symptoms that suggest respiratory problems

Features and symptoms	Problem indicated
Coughing, gagging, choking, congestion, and wheezing; symptoms can be associated with oral feedings or can occur chronically/intermittently	• Aspiration of food or liquid into the lungs • Increased mucus in the airways and lungs resulting from inflammation and infection
Episodes with increased coughing and congestion, increased work of breathing, and decreased oxygen saturation; symptoms improve with interventions to increase clearance of mucus from the lungs (such as chest PT, pulmonary vest, or insufflator-exsufflator cough production device)	• Mucus plugs and atelectasis, with resulting mismatch between the areas of the lung available for gas exchange with blood vessels (ventilation perfusion mismatch)
Recurrent episodes with increased respiratory secretions/mucus, coughing, wheezing, fever, increased respiratory rate, and increased work of breathing; often referred to as pneumonia or aspiration pneumonia	• Acute respiratory exacerbation, reflecting progression of inflammation and secondary infection, despite the use of chronic treatment (table 6.5) • Contributing problems noted in figure 6.2
Snoring, labored breathing during sleep, and episodes of increased effort of breathing associated with lack of airflow into the lungs, including pauses in snoring, often followed by a gasp with awakening	• Obstructive apnea
Pauses in breathing without respiratory effort	• Central apnea

higher risk for central hypoventilation and apnea. Commonly, parents notice gradual changes in their child. The information provided throughout this chapter can alert parents to potential respiratory problems.

TESTS FOR ASSESSING ACUTE AND CHRONIC RESPIRATORY ILLNESS

Diagnostic studies to evaluate the problems that contribute to respiratory illness in children who have SNI are summarized in table 6.3. In general,

TABLE 6.3 Tests to assess acute and recurrent respiratory problems

Study	Comments
Complete blood count (CBC), including a white blood cell count (WBC) Chest X-ray (CXR)	• WBC and CXR are used when evaluating an acute respiratory illness that suggests pneumonia, or when an acute illness is not improving with empirical antibiotic treatment • WBC and CXR are of limited benefit when a child who has SNI develops recurrent respiratory exacerbations and chronic symptoms as a result of multiple factors: How will the tests change a decision to treat the acute illness with an antibiotic and steroid? • See "Respiratory Home Management" (figure 6.4) for suggested guidelines when respiratory illnesses are recurrent, using clinical information to guide treatment decisions, rather than blood tests and CXR
Venous and arterial blood gas (VBG, ABG)	• Used to assess the risk of respiratory failure
Sputum cultures	• Sputum is not typically obtained in a manner that allows culturing of anaerobes, though anaerobes are often involved (Brook 2004) • Surveillance tracheal cultures are of limited value, given the change in bacterial flora from one culture to another (Cline et al. 2012) • Can be difficult to differentiate whether a positive tracheal culture represents "colonization" or "infection" (Rusakow et al. 1998)
Videofluoroscopic swallow study (VSS)	• Used to assess bolus formation, swallowing, and presence of aspiration with or without cough (Arvedson 2008) • Allows detailed feeding recommendations, including optimal feeding position and liquid consistency, such as liquids thickened to nectar, honey, or pudding consistency
Chest computed tomography (CT)	• Used to identify lung injury, such as in the diagnosis of bronchiectasis • Will this study change the treatment plan? Or will it document chronic changes without altering care plans or decisions?
Polysomnogram (sleep study)	• Used for diagnosis of sleep-disordered breathing • Evaluates for the presence of obstructive apnea, central hypoventilation, or central apnea
Gastroesophageal scintigraph ("milk scan")	• Used to measure reflux from the stomach into the esophagus and assess for the presence of aspiration, using a small volume of technetium-99m sulfur colloid

TABLE 6.3 *(continued)*

Study	Comments
	• Of limited use in the assessment of pulmonary aspiration (Baikie et al. 2005; Fawcett et al. 1988)
Radionuclide salivagrams (radiosialography)	• Used to detect aspiration of saliva, using a small volume of technetium-99m sulfur colloid (Boesch et al. 2006) • Minimal radiation exposure • No new information added if aspiration was previously documented by VSS
Bronchoalveolar lavage (BAL) with lipid-laden macrophage index (LLMI)	• Requires sedation or anesthesia for flexible bronchoscopy (Boesch et al. 2006) • LLMI considered to be of limited use

tests are used to assess acute respiratory illnesses and to identify what is contributing to the chronic and recurrent respiratory problems.

With any test, it is important to consider how the information gained will influence the child's treatment and care plans. As an example, though a chest radiograph (chest X-ray) can aid in the diagnosis of pneumonia, repeated use of a chest radiograph for a child who has SNI is of less benefit, especially because atelectasis and pneumonia can have similar findings on chest X-ray. Once the problems indicated in figure 6.2 are recognized, information from the child's history can help guide a decision to initiate an antibiotic. Ultimately, chronic and acute treatment are guided by an understanding of the multiple contributing problems that lead to acute respiratory exacerbations in children who have SNI.

When considering the available interventions for both chronic and acute treatment, it is important to recognize the potential to overstudy respiratory problems in children who have SNI. Asking "What will we do with this information?" can protect a child from repeated studies that do not change the care plan or the clinical course. Table 6.4 shows three examples of how information from diagnostic studies might guide decision making.

OVERVIEW OF THE TREATMENT OF RESPIRATORY PROBLEMS

My child has been treated several times for pneumonia. I want to make sure we are doing everything we can.

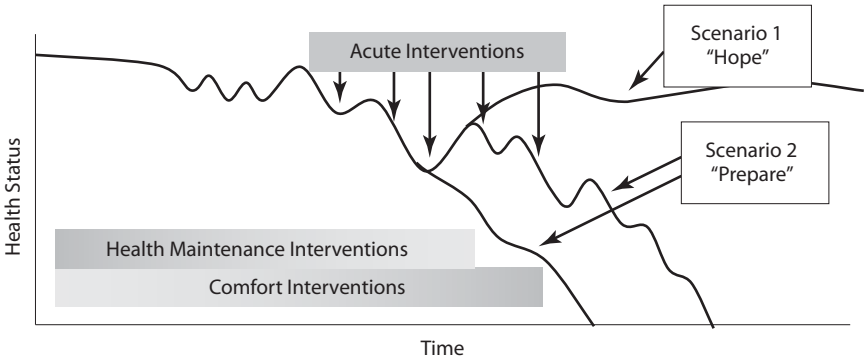
TABLE 6.4 Decision making based on tests for acute and chronic respiratory problems

Study	Information	Examples of decision making based on information
Videofluoroscopic swallow study (VSS)	Aspiration	• Initiate tube feedings • Discontinue oral feedings, except for taste and pleasure
Chest computed tomography (CT)	Bronchiectasis	• Information may support the "medical necessity" required for insurance coverage of equipment, such as a pulmonary vest • No future intubation, given an irreversible condition with ongoing decline despite optimal care • Continue to treat acute pulmonary exacerbations with antibiotics and steroids, as long as these are providing benefit without harm
Polysomnogram (sleep study)	Central apnea	• No tracheotomy, as this intervention will not alter the problem

In the following sections I review the medical interventions used for chronic and acute treatment of respiratory problems in children who have SNI, including surgical interventions and mechanical support of breathing. A framework for considering the potential benefit and harm of the available interventions is also provided.

Before reviewing the details of treatment options, it is worth reflecting on the broader scope and goals of treatment. Many of the problems that contribute to respiratory symptoms and illness in children who have SNI, such as impaired muscle tone and control and centrally mediated disordered breathing, are a result of impairment of the brain. This general consideration is not intended to focus on what cannot be "fixed" but rather to suggest how to frame the intended goals of acute and chronic treatment.

At its simplest, the goal of interventions, when the underlying primary problem cannot be removed, is to maximize the maintenance of health, minimize decline in health, and maximize recovery during acute respiratory illnesses. Many of the interventions reviewed here assist with meeting these goals, often over many years or decades. The challenges faced by families and clinicians are (1) deciding when an intervention is less likely to result in benefit or more likely to create harm and (2) determining when interventions are no longer having the intended and hoped for benefit.



Health maintenance interventions: Gastrostomy feeding tube, inhaled steroids, as-needed nebulizations, pulmonary vest

Acute interventions: Antibiotics, steroids, pulmonary vest, mechanical ventilation (BiPAP, invasive ventilation)

Comfort interventions: Fan, opioids, benzodiazepines, anticholinergics, feed to comfort, decrease fluids

Figure 6.3. Hypothetical respiratory trajectories *Used with permission of Oxford University Press; adapted from figure 26.2 in J. M. Hauer and K. W. Faulkner, "Neurological and Neuromuscular Conditions and Symptoms," in A. Goldman, R. Hain, and S. Liben (eds.),* Oxford Textbook of Palliative Care for Children, *2nd ed. (Oxford: Oxford University Press, 2012), p. 306.*

Figure 6.3 provides a framework for reflecting on a child's health journey. The goal is to utilize the "best" that medicine has to offer while minimizing the harm that might arise out of a sense of needing to "do something."

CHRONIC CARE: MAXIMIZE HEALTH MAINTENANCE AND MINIMIZE DECLINE

An overview of interventions for chronic, ongoing use is provided in table 6.5. These are described in more detail below.

Excessive respiratory secretions and mucus mobilization

When making decisions about the management of excessive secretions, it is helpful to consider sialorrhea (drooling) separately from thicker, respiratory secretions. Sialorrhea is the pooling of thin, watery secretions from the mouth as a result of a diminished oral sensation of saliva. There is ample evidence that medications such as glycopyrrolate and interventions to the salivary ducts can diminish sialorrhea.

TABLE 6.5 Chronic interventions and treatment

Intervention	Comments
*Improve mucus mobilization and clearance**	
Chest physiotherapy (chest PT) High-frequency chest wall oscillation (pulmonary vest) Insufflator-exsufflator cough production devices (CoughAssist)	• Pulmonary vest typically well tolerated • Insufflator-exsufflator not tolerated by all children • Equipment requires letter indicating medical necessity (i.e., a summary of health problems that indicate need) • No studies indicating one approach superior to another
Loosen secretions: mucolytic and mucoactive agents†	
Inhaled normal saline Inhaled hypertonic saline Inhaled dornase alfa (Pulmozyme) Inhaled *N*-acetylcysteine (Mucomyst)	• No studies in children or adults who have SNI • Dornase alfa recommended only for cystic fibrosis (CF); significantly lower concentration of mucus DNA in other airway diseases • Increased incidence of airway irritation and bronchospasm following dornase alfa and *N*-acetylcysteine
Decrease the development of inflammation and mucus	
Inhaled steroid: budesonide (Pulmicort), fluticasone (Flovent) Macrolides (see text discussion of antibiotics and anti-inflammatory activity)	• Inhaled steroids used empirically, based on chronic pulmonary inflammation associated with aspiration • No studies in children or adults who have SNI
Minimize or treat bronchospasm (constriction of the airways in the lungs)	
Inhaled short-acting beta-2 adrenergic receptor agonist: albuterol Inhaled anticholinergic: ipratropium (Atrovent) Inhaled long-acting beta-2 adrenergic receptor agonist: salmeterol (Serevent) Leukotriene receptor antagonist: montelukast (Singulair)	• Ipratropium and montelukast can also decrease secretion production, along with treating bronchospasm • Long-acting beta-agonists such as salmeterol may increase symptoms and increase the risk of death in some patients, as a result of bronchial inflammation and sensitivity; though they still have a role in the management of difficult-to-control asthma, their use has not been studied in children who have SNI (Chowdhury and Dal Pan 2010)

TABLE 6.5 *(continued)*

Intervention	Comments
Decrease fluid in the lungs (pulmonary edema)	
Diuretics Decrease total fluid intake given by feeding tube by 25% or more	• No evidence to indicate benefit from diuretics for recurrent respiratory exacerbations • Diuretics carry risk of electrolyte disturbances • Diuretic use should be reserved for patients with cardiovascular disease, such as for congestive heart failure • Children with limited activity may have an overestimation of daily "required" fluid needs (and water flushes after medications not always included)
Treat allergies	
Antihistamines: diphenhydramine (Benadryl), cetirizine (Zyrtec), loratadine (Claritin)	• Allergies may be suggested by seasonal symptoms and a family history of allergies, asthma, and/or eczema • Cetirizine, loratadine, and other second-generation antihistamines are less sedating
Decrease secretions	
Anticholinergics (see text discussion of secretions)	• Caution in drying up secretions too much
Assist with general symptom care	
Suctioning Oxygen	• Excessive suctioning can be an irritant and may increase secretion development • Oxygen well tolerated, though it can lead to overreliance on monitoring
Minimize infection in the lungs‡	
Vaccinations: influenza, pneumococcus Oral hygiene/dental care Inhaled antibiotics: tobramycin (TOBI) Prophylactic antibiotics–that is antibiotics to prevent infection (see text discussion of antibiotic treatment)	• No evidence that prophylactic antibiotics change outcome • Use of prophylactic antibiotics not recommended, given the lack of evidence and the associated risks (antibiotic resistance, diarrhea, *C. difficile*) • Risk of bronchospasm with inhaled tobramycin

(continued)

TABLE 6.5 *(continued)*

Intervention	Comments
	• Inhaled tobramycin may be beneficial for patients colonized with *P. aeruginosa*, studied mainly in patients with CF

Sources: Multiple sources, as noted.
*Homnick 2007; Miske et al. 2004; Plioplys, Lewis, and Kasnicka 2002; Schechter 2007; Yuan et al. 2010
†Fahy and Dickey 2010; Rogers 2007; Rubin 2007
‡Drobnic et al. 2005; Le et al. 2010; Rubin 2008

In contrast, an increase in respiratory secretions in children who have SNI can be a result of several mechanisms:

- *Impaired mobilization* of oral and pulmonary secretions
- *Inflammation* resulting in hypersecretion of pulmonary mucus, including inflammation resulting from chronic silent aspiration of oral secretions, underlying asthma, or development of bronchiectasis
- *Autonomic dysfunction* triggering increased secretion production
- *Clonazepam* use, associated with increased production of saliva and bronchial secretions (Browne 1978)

Management includes secretion mobilization with chest PT or pulmonary vest therapy (Plioplys, Lewis, and Kasnicka 2002; Schechter 2007; Yuan et al. 2010). There is no evidence that one intervention is superior to the other. The main difference is the convenience of pulmonary vest therapy (high-frequency chest wall oscillation). Both interventions tend to be well tolerated by children who have SNI. Another option is the insufflator-exsufflator cough production device (CoughAssist). Use of this machine involves placing a mask over the child's face. The machine applies positive pressure into the airway, followed rapidly by negative pressure. The rapid shift to negative pressure produces a high expiratory flow, simulating a cough. This device has been studied mostly for such diseases as spinal muscular atrophy (SMA) and Duchenne muscular dystrophy (DMD). Retrospective reviews suggest that it is tolerated and beneficial in minimizing pneumonia (Homnick 2007; Miske et al. 2004). However, it can potentially cause abdominal distension and worsen GER. Feedings should be withheld when this device is used. Experience indicates that not all children who have SNI can tolerate this machine.

Interventions to the salivary ducts or glands have variable results, though they may significantly decrease the frequency of suctioning for some children. Options include salivary duct ligation, excision of the salivary gland, or injection of botulinum toxin (Botox) into the salivary gland.

Some children have a decrease in secretions when autonomic dysfunction and pain, as a trigger for saliva production, are treated. Autonomic dysfunction may explain why frequent suctioning is associated with increased secretions in some children, with suctioning acting as the trigger.

Inhaled corticosteroids can decrease the development of pulmonary inflammation. A 5-day course of prednisone (along with an antibiotic) during acute respiratory exacerbations may provide additional benefit for a child with SNI and chronic aspiration of oral secretions who is experiencing more frequent exacerbations.

Nebulized normal saline may loosen secretions that are thick and difficult to mobilize. Nebulized hypertonic saline (3%) has proved effective for children who have cystic fibrosis (CF) but not for other conditions, such as chronic obstructive pulmonary disease (COPD). Mucolytic agents may help loosen and thin secretions, though these agents have mostly been studied in children who have CF. Such interventions include inhaled dornase alfa (Pulmozyme), which works by cleaving the DNA released by leukocytes in mucus, and inhaled *N*-acetylcysteine (Mucomyst), which severs the disulfide bonds of glycoproteins in mucus (Fahy and Dickey 2010; Rogers 2007; Rubin 2007). These interventions can result in bronchospasm. Dornase alfa is recommended only for treating CF, given the significantly lower concentration of mucus DNA in other airway diseases (Fahy and Dickey 2010).

Medications are available that decrease secretions, but they should be used with caution because they can result in thicker secretions that are more difficult to mobilize. Medications with anticholinergic properties that are used to decrease secretions include scopolamine, hyoscyamine, and atropine (Elman et al. 2005; Rapoport 2010). These are tertiary amines, which may cause sedation and delirium, as they are able to cross the blood-brain barrier. Glycopyrrolate, a quaternary amine that does not cross the blood-brain barrier, is another option and may be less sedating. No evidence exists to suggest that one medication is more beneficial or has fewer side effects than another. Finally, decreasing the total fluid intake by 25% or greater is a simple intervention to consider for management of excessive respiratory secretions.

A final related risk in children who have SNI is the development of fluid in the lungs, referred to as neurogenic pulmonary edema, if changes in the hypothalamus cause specific alterations in the autonomic nervous system.

Neurogenic pulmonary edema has been reported in people with brain tumors and multiple sclerosis, mostly described as developing at the end of life (Bramow et al. 2008; Macleod 2002). Though it has not been reported, experience indicates that neurogenic pulmonary edema may be relevant for a few children who have SNI; this condition may be suggested by a sudden and significant increase in saliva and pulmonary secretions.

Allergies may also contribute to secretions, because of nasal congestion. Allergies are suggested by symptoms that seem to occur seasonally. A family history of problems associated with allergies, including allergic rhinitis and asthma, would suggest an increased risk of allergies for a child in that family.

Justin is a 3-year-old who has SNI as a result of a near-drowning anoxic event 9 months ago. His current problems include daily episodes that suggest autonomic "storms" and/or central neuropathic pain. Episodes include stiffening, arching, facial flushing, and crying. He also requires frequent suctioning during these episodes, which appears to add to his agitation. He is currently treated with lorazepam, baclofen, and tizanidine for spasticity and agitation.

There is a significant decrease in the severity and frequency of these episodes with the addition of gabapentin and as-needed (prn) morphine sulfate. This treatment also corresponds to a significant reduction in secretions and need for suctioning. This decrease is noted within 2 weeks of starting gabapentin. All features, including tone, comfort, and secretions, are assessed to be more than 75% improved. The excessive saliva and secretions are thought to be secondary to autonomic dysfunction, with a decrease in secretions corresponding to a decrease in the other associated features. Baclofen and lorazepam doses are later decreased, without any change in Justin's comfort or tone.

Summary of interventions for respiratory secretions

- Factors that contribute to excessive respiratory secretions include impaired clearance of oral and pulmonary secretions, chronic inflammation, increased saliva production resulting from autonomic dysfunction, and a side effect of clonazepam.
- Chest physiotherapy and pulmonary vest therapy improve secretion/mucus clearance.
- The insufflator-exsufflator cough production device (CoughAssist) simulates cough and thereby improves secretion/mucus clearance.

- Salivary duct ligation or botulinum toxin (Botox) injection to the salivary duct can decrease the frequency of suctioning in some but not all children.
- Daily inhaled steroids and a 5-day prednisone course during acute respiratory exacerbations may decrease chronic inflammation.
- Anticholinergics, including glycopyrrolate (Robinul), scopolamine, hyoscyamine (Levsin), and atropine, can impair mucus clearance if secretions become too thick.
- Options for giving medications include a feeding tube, for all medications; sublingual/buccal (placing a small amount of liquid in the mouth), for hyoscyamine and atropine; and skin patch for scopolamine.
- Nebulized treatments to thin secretions:
  - Normal saline may loosen secretions that are thick and difficult to mobilize.
  - Other treatments have greatest benefit for people who have CF, with less benefit identified for other diseases, such as COPD and bronchiectasis.
  - Treatments include nebulized hypertonic saline (3%), inhaled dornase alfa (Pulmozyme), and inhaled *N*-acetylcysteine (Mucomyst). Dornase alfa is recommended only for people who have CF, as there is a significantly lower concentration of mucus DNA in people with other airway diseases. All of these treatments can result in bronchospasm.
- Decreasing total fluid intake by 25% or more can be beneficial: children with limited activity may have an overestimation of daily "required" fluid needs.
- Allergies should be treated, as suggested by seasonal symptoms and a family history of allergies.

ACUTE CARE WITH ANTIBIOTICS AND STEROIDS: MAXIMIZE RECOVERY

This section reviews interventions used to maximize recovery from acute respiratory exacerbations that result from chronic aspiration and impaired secretion mobilization. Acute care can include increasing the frequency of interventions used chronically, such as chest PT, pulmonary vest therapy, and bronchodilators, as discussed above. The use of antibiotics and steroids during these exacerbations is reviewed here.

Antibiotics

Antibiotic selection depends on the bacteria involved in aspiration. The site—home or hospital—where chronic and acute care are being delivered affects the type of bacteria causing respiratory infections: a child in a home setting and a child who has a prolonged hospital stay are exposed to different bacteria. The literature provides information on the bacteria involved in respiratory infections in children who have SNI:

- A report on aspiration pneumonia in 74 institutionalized children studied by transtracheal aspiration identified 5 types of bacteria isolated per sputum sample, with an average of 2.8 anaerobes and 2.2 aerobes (Brook and Finegold 1980). In this study, the predominant aerobic bacteria were alpha-hemolytic streptococci, *Streptococcus pneumoniae*, *Pseudomonas aeruginosa*, *Escherichia coli*, and *Klebsiella pneumoniae*.
- In another study, *S. pneumoniae*, *H. influenzae*, and Enterobacteriaceae predominated in patients with a community-acquired aspiration syndrome, whereas gram-negative organisms, including *P. aeruginosa*, predominated in patients with a hospital-acquired aspiration syndrome (Marik 2001).
- Studies of the bacteriology often fail to utilize anaerobic culture techniques, resulting in underreporting of anaerobic bacterial infections (Brook and Finegold 1980; Dreyfuss 2001).

Studies have identified the benefit of selecting antibiotics that include anaerobic coverage. In one study, a significant difference was noted in patients treated with ticarcillin-clavulanate or clindamycin, antibiotics with anaerobic coverage, compared with those treated with ceftriaxone (Brook 1996). Other studies found that clindamycin was comparable to ampicillin-sulbactam or panipenem-betamipron in the treatment of aspiration pneumonia, as well as having a lower incidence of post-treatment methicillin-resistant *Staphylococcus aureus* (MRSA) (Allewelt et al. 2004; Kadowaki et al. 2005). Other antibiotics used for the treatment of aspiration pneumonia include amoxicillin-clavulanate and levofloxacin (Marik 2001). It is important to note that levofloxacin can further increase the risk of seizures when used in combination with CYP1A2 substrate medications that increase seizure risk, such as mirtazapine and metoclopramide (Bellon et al. 2009).

The use of systemic prophylactic antibiotics in an attempt to avoid infection—such as using an antibiotic daily for 3 days each week, or 7 to 14 days each month—has been falling out of favor, given the lack of demonstrated benefit and the increase in antibiotic resistance. Other risks include development of *Clostridium difficile* or nonspecific diarrhea. Inhaled antibiotics, such as tobramycin, are another treatment to consider. Patients who may benefit from inhaled tobramycin are those colonized with *P. aeruginosa* (Drobnic et al. 2005; Le et al. 2010; Rubin 2008). The use of inhaled tobramycin carries a risk of bronchospasm (Drobnic et al. 2005).

Given the risk of developing bronchiectasis, it is also worth noting the bacteria identified in non-cystic fibrosis (non-CF) bronchiectasis. The most common organisms found in pediatric patients who have non-CF bronchiectasis are *H. influenzae*, *S. pneumoniae*, and *Moraxella catarrhalis*, with *P. aeruginosa* seen less commonly (Eastham et al. 2004; Goeminne and Dupont 2010; Stafler and Carr 2010). These organisms are similar to those found in patients with community-acquired aspiration pneumonia. The potential benefit of chronic inhaled antimicrobials, such as tobramycin, in treating non-CF bronchiectasis is less clear. In general, the prophylactic use of antibiotics is not recommended for patients with bronchiectasis.

The use of sputum and tracheal cultures must be considered and interpreted cautiously. Unfortunately, there are limited studies to guide a rational approach. A recent study of children with tracheostomy tubes concluded that the use of a prior tracheal culture was of limited value, given the change in bacterial flora from one culture to another (Cline et al. 2012). In addition, it is difficult to differentiate whether a positive tracheal culture represents "colonization" or "infection" (Rusakow et al. 1998). Finally, when a culture is obtained, it tells only part of the story, as sputum is not typically obtained in a way that allows anaerobes to be cultured (Brook 2004). As a result, a positive culture will steer one toward treating what is identified without considering the possibility of anaerobes. One approach is to empirically select antibiotics on a rotating basis when treating respiratory illnesses in the community, obtaining a culture when a child has a prolonged and complicated hospitalization.

Attention to oral hygiene may decrease the overall bacterial burden and thus decrease the frequency of respiratory infections. This has mostly been studied in the elderly population and in hospitalized patients. In general, poor oral health seems to increase the risk of pneumonia, as studied in adults residing in nursing homes and hospitals (Sjögren et al. 2008). To minimize this risk, the goal is to provide routine daily oral care along with regular dental visits, every 6 months.

In summary, aspiration pneumonia typically involves a mixture of aerobic and anaerobic bacteria. The bacteria most commonly isolated from individuals in home settings are those that live in the oral cavity. Enteric gram-negative bacilli and *S. aureus* are more common in respiratory infections that occur in the hospital. Antibiotic selection is empirical when a child who has SNI and chronic aspiration develops a respiratory exacerbation. Selection should be based on the patient's characteristics, the setting in which the acute respiratory exacerbation occurred, and available information on local pathogens and resistance patterns.

Children who have acute respiratory exacerbations with infection commonly have cough, wheezing, and increasing congestion, with or without fever. With the first few acute respiratory illnesses, a physical examination along with studies such as a chest X-ray can help guide a decision to initiate an antibiotic. As a pattern of recurrent respiratory exacerbations is established, a review of the child's clinical history can reveal when symptoms reflect a variation from baseline. For children who have SNI and recurrent respiratory exacerbations, as a result of the factors indicated in figure 6.2, there is a "tipping point" when infection is more likely to be contributing to the increasing symptoms. This tipping point can occur when an increasing bacterial load in the lungs overcomes the body's defenses for clearing infectious material. This can be suggested when symptoms worsen or fever develops. The goal is to balance initiation of an antibiotic close to this tipping point while minimizing overuse of antibiotics. Over time, the child's clinical history can help guide when treatment with inhaled medications and interventions for mucus clearance are "enough" to manage the contributing problems and when the information suggests an increasing potential for benefit from an antibiotic.

Summary of treatment for respiratory infections

- Attention to oral hygiene may decrease the load of bacteria in the mouth, with a subsequent decrease in bacteria intermittently entering the lungs.
- Antibiotics to consider for recurrent respiratory exacerbations as a result of recurrent aspiration in children and adults with SNI:
  - *Home/community setting at the time of respiratory illness:* amoxicillin-clavulanate (Augmentin), clindamycin (Cleocin), and fluoroquinolones such as ciprofloxacin and levofloxacin (Levaquin)
  - *Repeated hospitalization:* ampicillin-sulbactam (Unasyn), piperacillin-tazobactam (Zosyn), ticarcillin-clavulanate (Timen-

tin), imipenem, fluoroquinolones, and third-generation cephalosporins

- Inhaled tobramycin is another possible home-based option, though there is less evidence to support its use for children with non-CF pulmonary disease. It carries a risk of bronchospasm.
- Prophylactic antibiotics—that is, antibiotics given for a prolonged period in an attempt to prevent infection—are not routinely recommended, due to such problems as nonspecific diarrhea, diarrhea due to *C. difficile* infection, and development of antibiotic resistance.
- This discussion does not list all potential antibiotics that might reasonably be used for recurrent respiratory exacerbations with associated aspiration in children who have SNI. Rather, it focuses on the different settings of care and the antibiotics most commonly recommended. It includes antibiotics that can be given by feeding tube, ensuring options that can be part of home care plans. Such plans may have the benefit of minimizing the risk of hospital-acquired infections (nosocomial infections) associated with repeated hospitalizations. As reviewed throughout this book, the goal is to ensure that families have comprehensive information about options, as they weigh the risks and benefits of care plan choices for their child.

Anti-inflammatory treatment including steroids

Both chronic use of inhaled steroids and short-course steroid treatment at times of acute respiratory exacerbations have become more common. Theoretically, incorporating steroids into chronic and acute care plans addresses the inflammation that is part of chronic aspiration and impaired secretion mobilization. Unfortunately, there are limited studies that evaluate the use of steroids for these respiratory problems. The limited information we do have suggests some benefit, including a randomized, double-blind, placebo-controlled trial of methylprednisolone use for 30 adults with aspiration pneumonia. All patients received clindamycin for 3 days. The group that received methylprednisolone showed a statistically significant improvement in all parameters monitored, compared with the group receiving placebo (Hatakeyama et al. 1995). In a rat model study evaluating the effect of hydrochloric acid aspiration, steroids were found to inhibit the inflammatory process in the lungs after acid aspiration (Nagase et al. 1991). One case report of a child with SNI and chronic aspiration found

some benefit with a combination of antibiotics and prednisone during acute respiratory exacerbations (Hauer 2007).

With this limited information, we can conclude that there may be benefit from a 5-day course of oral prednisone during acute respiratory exacerbations in children with chronic aspiration and increasing frequency of respiratory exacerbations. The addition of a prednisone burst, along with an antibiotic, for the treatment of an acute respiratory exacerbation can be considered when a child with SNI and chronic aspiration has been treated with an antibiotic for three or more respiratory exacerbations in a year, when an exacerbation occurs within 2 to 3 months of the last exacerbation treated with an antibiotic, or when there is a strong family history of asthma.

Macrolides such as azithromycin may have an added benefit, given their anti-inflammatory activity. Treatment approaches include daily dosing, three times per week, and short-term acute use. Studies in children have focused on patients with diseases such as CF and asthma, with positive yet variable results (Amsden 2005; Shinkai and Rubin 2005). There is insufficient evidence for the use of macrolides in bronchiectasis (Stafler and Carr 2010). There are no studies to suggest routine use for children who have SNI and chronic aspiration, beyond the known antibacterial coverage, such as against *H. influenzae*, *S. pneumoniae*, *M. catarrhalis*, and *Mycoplasma pneumoniae*, with less activity against oral anaerobes. Risks associated with chronic use include antibiotic resistance, diarrhea, *C. difficile*, and hearing loss.

When considering a treatment that has been studied for other diseases, as in the example of macrolides, it may help to frame decisions by considering the number of contributing factors for each disease. To illustrate: children who have SNI commonly have three or more problems that contribute to respiratory illness and decline, including impaired mucus mobilization, microaspiration with inflammation and infection, and restrictive lung disease. In contrast, children with diseases such as asthma or CF can be considered to have one contributing problem. As a result, any treatment benefit identified for asthma or CF would be beneficial for only one of the contributing problems in children who have SNI—that is, for a child with SNI, any benefit may be 25% to 30% or less of that seen for a child with asthma or CF. This information can help when weighing the potential benefit with the known risk. For this reason, macrolides may be best reserved as a treatment option for an acute respiratory exacerbation, to avoid associated risks from chronic use.

Summary of treatment for lung inflammation

- Daily inhaled steroids can include budesonide (Pulmicort) or fluticasone (Flovent).
- Prednisone, for a 5-day course, can be used with an antibiotic for recurrent respiratory exacerbations.
- Macrolides such as azithromycin (Zithromax) may have a theoretical benefit, given their anti-inflammatory activity, but have not been studied in children with SNI and are not as effective against the bacteria involved in chronic aspiration.
- When considering an intervention with unknown benefit, it can help to consider that any treatment benefit identified for a disease with one factor that contributes to impaired respiratory health, such as asthma or cystic fibrosis, will be less for a child who has SNI. Children with SNI commonly have three or more problems that contribute to respiratory illness and decline, such as impaired mucus mobilization, shallow breathing as a result of limited activity, microaspiration with inflammation and infection, and restrictive lung disease. As a result, the potential benefit of the treatment is less, yet the associated risks are the same.

SURGICAL INTERVENTIONS: IMPROVE HEALTH AND MINIMIZE DECLINE

Surgical interventions are typically considered only after many of the chronic and acute interventions have been utilized or when a specific problem has been identified, such as NM scoliosis. When considering a surgical intervention, it is essential to determine whether the intervention will relieve a problem or whether there are other contributing problems that will remain, thus lessening the intended benefit. Evidence, though limited, provides a foundation of important information. The cases of Sofia, Jenay, and Danny (see "Case examples") highlight decision making for some of these interventions. Table 6.6 summarizes surgical approaches to treatment.

Nissen fundoplication

Nissen fundoplication is a specific type of anti-reflux surgery (ARS) that involves surgical tightening of the junction between the stomach and the

TABLE 6.6 Summary of surgical interventions

Intervention	What is it?	Comments
Nissen fundoplication (anti-reflux surgery)	Surgical tightening of the junction between the stomach and esophagus, to prevent reflux of stomach contents into the esophagus	• Problems following this procedure include retching (gagging, dry heaves), decreased ability of the stomach to tolerate the same volume of feeding, and pain localized to the abdomen • A trial of jejunal (J-tube) feedings can be considered prior to the Nissen procedure • May decrease respiratory symptoms, though unclear whether there is any long-term benefit for respiratory exacerbations (pneumonia, aspiration pneumonia)
Salivary duct ligation or botulinum toxin injection	Ligation of the salivary duct, excision of the salivary gland, or injection of botulinum toxin (Botox) into the salivary gland	• Can decrease the amount of suctioning needed for some patients, but may not alter the long-term frequency of respiratory exacerbations • Effect of Botox may last 3–6 months, though some patients benefit for only several weeks
Tracheotomy	Creation of an airway through the neck into the trachea (windpipe), with placement of a tracheostomy tube	• Significantly greater benefit for conditions of airway obstruction, such as with a craniofacial abnormality • Sometimes presented as a benefit to "pulmonary toilet," though this benefit is limited to suctioning, without any change in mucus production and clearance (see text discussion of management of secretions)

TABLE 6.6 *(continued)*

Intervention	What is it?	Comments
Tracheal separation or diversion	Separation of the trachea (windpipe) into an upper section that remains a blind pouch, or is connected to the esophagus, and a lower section that becomes the new airway with a tracheostomy tube	• Eliminates a child's ability to vocalize: "I won't know if he is upset when I am not in the room with him" • One study found that 21% of children died during the follow-up period of 1 month to 5 years (see text discussion)
Spinal surgery	Surgery to correct excessive curvature of the spine	• Unclear how much benefit in eliminating this cause of restrictive lung disease in children who have SNI (see text discussion); the benefit is probably greater for children without other contributing problems to respiratory health

esophagus, in an attempt to prevent acid reflux. Data have established the benefit of ARS for problems that result from GER despite treatment with medications, including vomiting, esophagitis (inflammation of the esophagus), and hematemesis (vomiting of blood).

In contrast, ARS has not been demonstrated to produce a significant decrease in the frequency of pneumonia in children who have SNI, though it is often considered for this purpose (Cheung et al. 2006; Goldin et al. 2006; Kawahara et al. 2004; S. L. Lee et al. 2008; Smith et al. 1992). A retrospective observational cohort study of children with neurological impairment and first fundoplication did find a reduction in hospitalization rate for aspiration pneumonia in children less than 3 years of age. For all children, the hospitalization rate for those diagnosed with pneumonia stayed the same, and it increased for those diagnosed with asthma (Srivastava, Berry, et al. 2009). In this study, it is important to note that children older than 3 years had an increase in reflux-related hospital admissions, including for aspiration pneumonia. In addition, almost two-thirds of all children in the study received a gastrostomy feeding tube (G tube) at the time of fundoplication. It is not possible to know whether the decrease in hospitalization for aspiration pneumonia in the younger patients was a result

of the fundoplication or the elimination of oral feedings following G-tube placement. There have been a few studies comparing fundoplication with a gastrojejunal (GJ) feeding tube, with no difference in outcomes identified (Srivastava, Downey, et al. 2009; Wales et al. 2002), including no difference in the time to develop aspiration pneumonia or in mortality rate.

As a reminder, a number of other factors contribute to respiratory problems in children who have SNI that are not altered by ARS, which may account for the unclear benefit of ARS for prevention of future "pneumonia" or "aspiration pneumonia." In addition, children who have SNI are at higher risk for complications following ARS, such as the development of retching, impaired gastric accommodation (ability of the stomach to tolerate the same volume of feeding), and pain localized to the abdomen (Di Lorenzo and Orenstein 2002; Mousa et al. 2006; Richards et al. 2001; Smith et al. 1992). These are important considerations to factor into a decision to proceed with ARS.

Salivary duct ligation or botulinum toxin injection

Salivary duct procedures have been found to decrease drooling in children with neurological impairment. However, salivary duct ligation with or without submaxillary gland excision as a treatment for chronic aspiration did not alter the frequency of lower respiratory tract infections in a retrospective review of 62 children with pulmonary aspiration (Vijayasekaran et al. 2007). Another study looked at outcomes after botulinum toxin injection, over a shorter period of follow-up. The numbers of pulmonary infections and hospitalizations before and after the procedure were obtained through telephone interviews with parents. Though a decrease in infections and hospitalizations was reported, the data were from the nine patients with reported benefit, with no further information on the three children without benefit (Raval and Elliott 2008). Of note, this intervention significantly decreased the reported frequency of suctioning in some patients.

Salivary duct interventions are best considered as potentially benefiting secretion management and minimizing the use of anticholinergic medications. These interventions are unlikely to alter the long-term risk of respiratory exacerbations in children with multiple contributing factors.

Tracheotomy

A tracheotomy is the creation of an airway through the neck into the trachea (windpipe) with placement of a tracheostomy tube. The terms *trache-*

otomy and *tracheostomy* are often used interchangeably. A tracheotomy is indicated for treating obstruction of the airway or for prolonged mechanical ventilation. In a retrospective review comparing outcomes following a tracheotomy, neurologically impaired children had a mortality rate of 27%, compared with 11% or less for children with conditions of airway obstruction (Carron et al. 2000). Specifically, the mortality for children with upper airway obstruction was 11%; vocal fold paralysis, 8%; and craniofacial abnormality, 0%. The different mortality rates probably reflect a greater benefit for airway obstruction and less benefit for children who have SNI and respiratory compromise resulting from multiple factors. This conclusion is further supported by a retrospective review of outcomes following tracheotomy (Berry et al. 2009).

Tracheostomy does not improve secretion management or decrease aspiration of oral secretions. Complications with a tracheostomy include bleeding, obstruction of the tube by mucus, and an increased frequency of respiratory infections, given that the tracheostomy bypasses the natural defenses of the upper airway that filter out debris and bacteria. Detailed information for parents about the daily care of a tracheostomy, along with other information, is available at www.tracheostomy.com.

Tracheal separation or diversion

Laryngotracheal separation (LTS) or diversion has been identified as a surgical intervention to eliminate chronic aspiration of oral secretions. In a series of 19 neurologically impaired children retrospectively reviewed following LTS, 14 had previous tracheotomies and 17 had previous ARS surgery (Cook, Lawless, and Kettrick 1996). Four patients (21%) died following surgery, with follow-up ranging from 1 to 62 months, but none died as a consequence of the surgery. A more recent review had similar findings (Zocratto et al. 2006). Evidence is lacking for the long-term benefit of this procedure for children who have SNI. In addition, LTS eliminates a child's ability to vocalize, a feature that some parents find too burdensome for their child: "I won't know if he is upset when I am not in the room with him."

Mandibular distraction

Mandibular distraction has been most studied in children with craniofacial abnormalities, such as severe micrognathia (small jaw), that result in significant airway obstruction (Genecov et al. 2009; Mandell et al. 2004).

This intervention probably has limited utility for children with multiple factors contributing to respiratory problems.

Spinal surgery

Spinal surgery for NM scoliosis—that is, scoliosis resulting from muscle weakness, abnormal muscle tone, and abnormal posture—was reviewed in 288 children who had cerebral palsy (Tsirikos et al. 2003). The average age at the time of surgery was 13 years 11 months (SD 3 years 4 months). Mortality was 12.5%, which included 3 deaths around the time of surgery, 33 other deaths with a mean postsurgical survival of 4.3 years, and a mean estimated survival of 11.2 years for all patients. Missing from this analysis was a stratification of patients based on their pulmonary status prior to surgery and a review of anticipated survival without surgery.

DECISION MAKING WHEN AN INTERVENTION ADDRESSES ONLY ONE OF SEVERAL CONTRIBUTING PROBLEMS

The surgical interventions reviewed above highlight an important point, touched on earlier and worth repeating: children with multiple problems contributing to their chronic respiratory symptoms and acute exacerbations will not have the same benefit from an intervention addressing only one of those problems as will children with a single problem that is addressed by that intervention. It is beneficial to factor this information into decisions about any intervention. A useful strategy is to create a scale from 1 to 10, with 1 indicating a single contributing factor, 5 indicating a few contributing factors with some compromise in health, and 10 indicating multiple contributing factors with a significant decline in the child's baseline health (table 6.7). Parents can reflect on their child's health and on whether there has been any decline, and then estimate whether their child's current baseline is 25% less, 50% less, or more than 50% less than when at its best. A specific number is not important; what's important is the benefit of recognizing a child's overall decline as "none," "a little," or "a lot."

This strategy provides a framework for families as they consider the likely benefit and risk of any intervention. Decision making can also be framed by recognizing the relative contribution of each problem. When an intervention is recommended, it can be considered in terms of relative benefit. For example, for a child with anatomical airway obstruction and no other contributing problems, the identified problem is essentially con-

TABLE 6.7 Considering the benefit and risk of a surgical intervention, with examples

1 (higher benefit, lower risk)	5	10 (lower benefit, higher risk)
No decline in health	A little decline in health	A greater decline in health
The intervention will address the single contributing problem.	There are several contributing problems.	The intervention will address only one of many contributing problems.
Tracheotomy	*Tracheotomy or spinal surgery*	*Tracheotomy, anti-reflux surgery, spinal surgery, laryngotracheal separation*
For a child with congenital anomalies and anatomical airway obstruction with no other contributing problems	For a child with some contributing factors, infrequent respiratory exacerbations, and less decline in health than a child rated "10"	For a child who has SNI and associated aspiration of secretions, less-effective cough, neuromuscular scoliosis, mild obstructive apnea, and respiratory exacerbations every 2–3 months, with declining benefit from chronic and acute treatments, and a gradual but significant decline in health
Spinal surgery for scoliosis		
For a child with cerebral palsy and neuromuscular scoliosis with no other health problems (no aspiration, airway obstruction, or history of respiratory symptoms or illness)		

tributing 100% to any compromise in the child's respiratory health. In contrast, for a child who has multiple contributing problems, the family and medical team can estimate the relative contribution of each problem. This approach to considering an intervention for compromised respiratory health ensures that problems that cannot be "fixed" will be recognized—such as impaired clearance of secretions, chronic aspiration, chronic inflammation, and shallow breathing.

Parents are often the greatest experts in such a process. Some questions can help families in utilizing their expertise: Is the decline in health greater than the potential benefit from the intervention? Is scoliosis contributing less to any respiratory compromise than is the combination of the other multiple problems? In addition, any estimated decline in the child's health allows a family to consider the increased risk that may be associated with surgery. Outlining and discussing such a process helps empower the parent as the expert in the child's health problems. Families may then frame their decisions as "I wish for my daughter to have this chance at a benefit" or "I can't risk putting my son through this surgery, given what we know about him and wish for him."

For a child with multiple contributing problems and a decline in health, considering a tracheotomy is best done in conjunction with considering mechanical ventilation, even when the need for such support is not immediate. This recommendation reflects the limited likelihood of benefit to respiratory health from a tracheotomy procedure in such a child and, therefore, seeing the use of chronic ventilation as the other reason for a tracheotomy. If this has not been anticipated and discussed, parents may feel obligated to utilize mechanical support once their child has a tracheotomy. Yet it also helps to recognize that initial considerations and decisions can change as experiences change.

In this example of thinking about the role of mechanical ventilation, the goal is not to come to a final decision about use but rather to factor this use into a consideration of the benefit and risk of a tracheotomy. As examples of decisions, one family may not wish to use mechanical support in the future but may see a tracheotomy as a benefit for airway clearance of secretions; another family may not wish to use mechanical support and may see the risk of a tracheotomy as greater than any potential benefit; and another family may feel that they will be better able to make a decision about mechanical support "when that time comes" and thus defer any decision about a tracheotomy until that time.

ADDRESSING RESPIRATORY DISTRESS

Dyspnea is the experience of shortness of breath, difficulty breathing, breathlessness, or uncomfortable breathing. It is a common symptom of numerous respiratory disorders, including diseases of the lung parenchyma and obstruction of the airway, as can result from repeated microaspiration with resulting infection, inflammation, bronchiectasis, and fibrosis over time.

Dyspnea should be considered when a child who has SNI is experiencing more frequent, recurrent respiratory exacerbations. Interventions that minimize associated distress can be instituted while still using treatment for the chronic and acute contributing problems of inflammation and infection. Interventions that minimize distress become essential when the primary goal of treatment shifts to comfort.

Identifying dyspnea in nonverbal children who have SNI

Measures of respiratory rate, oxygen saturation, and blood gas levels do not necessarily correlate with a person's perception of breathlessness. To assist with assessment of dyspnea in adults unable to report symptoms, the Respiratory Distress Observational Scale (RDOS) was developed (Campbell 2008; Campbell, Templin, and Walch 2010). Though this tool is not recommended for use in children without further study, it suggests information that can be useful when assessing for dyspnea in nonverbal children who have SNI. Parameters assessed by this tool include heart rate, respiratory rate, use of accessory muscles, paradoxical breathing pattern with use of abdominal muscles, appearing restless, fearful facial appearance, grunting at the end of expiration, and nasal flaring (Campbell 2008, 2010; Campbell, Templin, and Walch 2010). One caution in using this information is the recognition that for patients able to self-report, respiratory rate does not always correlate with the perception of breathlessness. This is especially important in younger infants who may have compensated tachypnea (increased respiratory rate) without any further obvious distress.

Parents can assess for dyspnea in a nonverbal child by using strategies similar to those used in pain assessment. To start, parents can consider whether they have observed their child to be in distress or to appear anxious during recurrent respiratory exacerbations. The child's specific behaviors can then be identified and documented. These behaviors may include an altered facial expression such as grimacing, having an anxious or fearful look, appearing restless, or becoming withdrawn. Other observable information may include flaring of the nostrils (nasal flaring), grunting, and use of the muscles between the ribs (accessory respiratory muscles), signs indicating increased work of breathing. As with pain assessment in children who have SNI, parents and other caregivers can be empowered with information that helps them identify distressed breathing in a child.

Treatment

When children who have SNI and recurrent pulmonary exacerbations are observed to be in distress during a respiratory illness, the focus is typically on treating the underlying cause. It is also beneficial to integrate symptom management into the care plan, in the same way that pain treatment is used for cancer patients while treating the source of pain. Evidence has identified several interventions that decrease distress from dyspnea, including as part of treatment plans for chronic diseases of the lung; examples include adults with severe lung disease, such as COPD. These interventions include an oxygen trial, cool air from a fan or open window, repositioning, morphine sulfate, and benzodiazepines for associated anxiety.

Airflow from a fan and oxygen

A fan that directs airflow across the mouth and nose has been shown to reduce the sensation of breathlessness (Galbraith et al. 2010). This benefit may be mediated by stimulation of the thermal and mechanical receptors of the trigeminal nerve of the face. Oxygen use may decrease uncomfortable breathing for some people who have dyspnea, though in a double-blind, randomized controlled trial it provided no greater benefit over room air for adults with life-limiting pulmonary illness (Abernethy et al. 2010). In addition, there is no correlation between a person's oxygen saturation and perception of breathlessness. When oxygen is used for people who have dyspnea, the focus must be on the observed benefit for the patient, not on the oxygen level.

Morphine sulfate

Morphine sulfate is beneficial in treating dyspnea through several potential mechanisms, including a decrease in the perception of uncomfortable breathing, a decrease in oxygen consumption, and vasodilation resulting in reduced pulmonary congestion. Morphine sulfate has been most thoroughly studied in adults with dyspnea due to severe, chronic lung disease, such as COPD. In a randomized, double-blind, placebo-controlled crossover trial, participants had significant improvement in dyspnea with morphine sulfate, with no concerning episodes of sedation (Abernethy et al. 2003). Other studies have also found a benefit with the use of morphine, without development of respiratory depression, for the management

of dyspnea that occurs despite maximal treatment of the underlying cause (Allen et al. 2005; Clemens and Klaschik 2007; Mazzocato, Buclin, and Rapin 1999). A suggested starting dose for someone not taking an opioid is 25% to 30% of the dose used for pain. Morphine sulfate is the most studied, though other opioids can be used at equivalent doses.

Morphine can provide benefit by using as needed. When respiratory distress is noted on most days, or when as-needed (prn) doses are used more than twice a day for several days, it can be beneficial to provide morphine on a scheduled basis. Further information on the use of morphine sulfate is given in chapter 4. The case of Eva, at the end of chapter 9, illustrates the benefit of scheduled morphine as respiratory distress becomes more frequent.

The fear of using an opioid for an individual who has chronic lung disease is understandable, yet is unwarranted. Opioid-induced respiratory depression is unlikely with appropriate dosing and titration, including a starting dose of morphine for dyspnea that is one-fourth to one-third of the dose used for pain. This initial starting dose can be lowered for children with a decreased level of alertness or a history of oversedation from a routine starting dose of other medications. The starting dose can be increased by 30% to 50% if there is no benefit from the initial dose.

One possible caution is morphine use for children with severe hypotonia and limited "effort" noted during respiratory illnesses. Such children may have less reserve of muscle activity and greater risk with sedating medications. This is in contrast to children who have SNI and increased muscle tone, with an active "effort" noted during a respiratory exacerbation. Though muscle tone is not the same as strength, hypotonia at rest results in muscles that are slower to contract and less able to maintain a contraction. Such children still deserve symptom treatment; caution doesn't mean not using morphine. Until this distinction is studied, one can begin with a lower starting dose, such as one-sixth to one-fifth the dose used for pain, and then increase if there is no benefit from the initial dose.

Adverse effects of opioids, such as sleepiness, are infrequent, and patients quickly develop tolerance to these side effects. In fact, any transient sedation that occurs may be related to making up for prior disrupted sleep that resulted from the discomfort of dyspnea. Finally, patients whose symptoms are successfully managed may have improved survival due to a reduction in physical and psychological stress and exhaustion (Temel et al. 2010).

Nebulized morphine sulfate is not recommended for dyspnea, though case reports suggest that some individual patients may benefit (S. J. Brown,

Eichner, and Jones 2005). In general, it is considered ineffective for the treatment of dyspnea resulting from chronic lung disease and has the added risk of causing bronchospasm. For these reasons, opioids for the treatment of dyspnea should be given by mouth, feeding tube, or IV line.

Benzodiazepines

Benzodiazepines are another pharmacological option for management of dyspnea. Their benefit is primarily through managing anxiety associated with dyspnea. Because they do not reduce dyspnea directly, they should not be the only medication used. Instead, they should be considered second-line therapy when symptoms persist, such as using along with morphine sulfate (Simon et al. 2010). Studies have identified the combination of morphine and a benzodiazepine as safe and beneficial in the treatment of dyspnea (Clemens and Klaschik 2011; Navigante et al. 2006). Benzodiazepine options include midazolam and lorazepam. Midazolam has the advantage over lorazepam of faster onset and shorter duration, thus avoiding prolonged sedation.

Improved health in some children following symptom treatment

Some children are found to have better oxygenation when dyspnea is improved with morphine sulfate. An increase in the work of breathing, as occurs with dyspnea, can increase the metabolic rate, resulting in an increased oxygen requirement. In addition, breathing may be less effective at such times, including the tensing of muscles resulting in poorly coordinated breathing (Hauer and Mackey 2012). Just as the goal to improve health with medical treatment (antibiotics and prednisone) can secondarily improve comfort earlier in a child's health trajectory, the goal to improve comfort with morphine and other interventions can sometimes secondarily improve health.

Integrating symptom treatment into medical care plans

Respiratory distress during respiratory exacerbations is an underrecognized symptom in children who have SNI. It is beneficial to consider symptom management strategies for these children as respiratory exacerbations occur with increasing frequency. Morphine sulfate is included in the "Respiratory Home Management" plan (discussed below; see figure 6.4) as a reminder to consider distress during recurrent respiratory exacer-

bations and to include this medication in care plans when distress is recurrent (Hauer 2007). This approach is consistent with the integration of dyspnea management into care plans for adults who have severe lung disease and persistent dyspnea, such as those with COPD. It allows symptom management to be integrated into acute medical care plans in advance of seeing limited benefit from chronic and acute medical treatment.

Waiting until the goal is "comfort care" rather than "treatment" delays the start of strategies that improve comfort. The potential for dyspnea should be considered as the number of days with significant respiratory symptoms increases, such as when the frequency of respiratory exacerbations has increased to every 3 to 4 months.

Reviewing the role of respiratory distress and its management options can help with future decision making. The goal is to make sure that comfort is part of the care plan, to minimize decisions to use interventions because of fear of suffering. The cases of Nathan (below) and Derick and Jonathan (in "Case examples") highlight the benefit of symptom treatment plans that address dyspnea.

Summary of assessment and management of respiratory distress

- Dyspnea is uncomfortable breathing, respiratory distress, and shortness of breath.
- Information that suggests dyspnea in a nonverbal child with recurrent respiratory exacerbations includes anxious facial appearance, facial grimacing, appearing restless, grunting sounds, flaring of the nostrils, appearing to work harder to breathe, and use of muscles located between the ribs.
- The level of oxygen saturation does not correlate with a person's feeling out of breath.
- For children who have SNI and recurrent respiratory exacerbations, symptom management can be used along with acute treatment (see "Home care plans" below).
- Interventions that can decrease the sense of uncomfortable breathing include a fan with airflow directed at the face, repositioning, and a calm environment; medications include morphine sulfate and a benzodiazepine.
- The use of morphine sulfate has been studied in adults who have severe pulmonary disease, such as COPD, with reports identifying significant improvement in dyspnea with no episodes of significant sedation or respiratory depression.

- The starting dose of morphine sulfate is 25% to 30% of the dose used for pain, another factor contributing to its safety for a child who has an acute respiratory illness. A lower starting dose can be used for children with significant sedation or severe hypotonia.

Nathan is a 10-year-old boy who has lissencephaly and associated microcephaly, cerebral palsy, and intellectual impairment. He is currently treated in the hospital every 2 to 3 months for recurrent respiratory exacerbations. During the most recent admission, Nathan was intubated and placed on mechanical ventilation for management of respiratory failure. There had been no previous discussions to prepare Nathan's family, who later shared that it was hard to know what they would have decided if they had been asked.

Nathan remains intubated 1 week later. The palliative care team is consulted to assist his family and learns that Nathan has had an overall decline in health, along with diminishing benefit from chronic and acute treatments. An earlier evaluation of Nathan included a sleep study that ruled out obstructive apnea, persistent O_2 sats to the mid-80s, normal findings on an upper gastrointestinal (UGI) series, and decreased lung volumes noted on chest X-ray. Nathan has been fed by G tube most of his life and had a Nissen fundoplication at 7 years of age.

A team meeting is arranged to include Nathan's primary physician, pulmonologist, and the intensive care physician, as well as members of the pediatric palliative care team. The family is presented with options and an expectation that if Nathan is able to recover to extubation, it will occur within 1 to 1½ weeks. The family does not anticipate Nathan having surgical interventions such as a tracheotomy or home ventilation, though they wish to explore the information discussed. A plan is arranged to meet with the family in 1 week, allowing them time to consider their options, with ongoing support to be provided in the interim.

During this time, the family and care providers identify the following goals as most important when making any decisions for Nathan: his comfort, quality of life, and the opportunity to remain at home, where he is happiest. Family and home care nurses continue to hope for recovery and as much time as possible with Nathan. Nathan is extubated the day before the next meeting. During this meeting, the family members discuss what they would want for Nathan when the next respiratory illness occurs. They feel they understand what medical interventions in the hospital can and cannot do for Nathan. They also understand the home care plan outlined earlier and how hospice can assist with their goals of maintaining Nathan's comfort and care at home.

For Nathan's family, the most distressing decision is to forgo the use of intubation in the future. Given the length of time Nathan has been on the venti-

lator, they anticipate that this will only get worse and that the next time "he might not get off and we don't want him hooked up to machines." They also find the home care plan helpful in considering their options: "We can continue to treat him for as long as it is helpful but allow him to be at home."

During the next respiratory exacerbation, the home care plan is used, including morphine sulfate along with an antibiotic and prednisone. Nathan's family is amazed at how much more comfortable he appears during this illness. They are also delighted that he has improved from this acute illness. They now feel more certain about their goals for Nathan and feel prepared for the time when the home treatment plan may no longer benefit him, but certain that they can maintain his comfort throughout life, with guidance in adjusting doses as needed.

Home care plans

The "Respiratory Home Management" plan (figure 6.4) outlines chronic and acute home care strategies, based on experience and evidence, for children who have SNI and recurrent respiratory illnesses. Using a home care plan can be beneficial when a child with known risk factors for recurrent respiratory illness is being treated more frequently with antibiotics and steroids. A review of each prior episode can often identify a pattern of symptom progression that did not reverse with inhaled medications, suctioning, and mucus mobilization. Criteria for initiating acute treatment with an antibiotic and prednisone can then be defined. The following instructions are an example of information that can help guide a family:

1. Increase pulmonary vest therapy and budesonide (Pulmicort) to four times per day when the following symptoms persist or worsen: cough, wheezing, secretions, congestion.
2. Initiate the prescribed antibiotic and prednisone when the above symptoms worsen or do not improve within 1 to 2 days, or if fever develops.
3. Call the clinic [phone number] the next day to update our team.
4. We will provide your pharmacy with a new prescription after each illness.
5. Call if you have any concerns: [phone number] during clinic hours, or [phone number] after hours, and ask for the physician on call for the Complex Care team [team name].

HOME CARE PLAN FOR FAMILIES

Respiratory Home Management: Medical Treatment and Comfort Strategies

Name _____
DOB _____
Weight _____

Daily Care: Chronic Treatment

As needed

- ☐ Suctioning
- ☐ Saline or hypertonic (3%) saline nebs
- ☐ Oxygen as directed by oximeter reading or appearance
- ☐ Other _____

Every 4 hrs as needed for cough, wheeze, congestion

- ☐ Albuterol nebs
- ☐ Ipratropium (Atrovent) nebs
- ☐ Duoneb (albuterol and ipratropium) nebs
- ☐ Other _____

2 times per day and as needed

- ☐ Chest physiotherapy (CPT) OR high-frequency chest wall oscillation (vest therapy)
- ☐ Insufflator-exsufflator (CoughAssist)

2 times per day

- ☐ Steroid nebs: budesonide (Pulmicort) or fluticasone (Flovent)

Daily

- ☐ Histamine-2 receptor blocker or proton pump inhibitor for gastroesophageal reflux
- ☐ Antihistamine: diphenhydramine (Benadryl), cetirizine (Zyrtec), etc.
- ☐ Leukotriene receptor antagonist (Singulair)

Sick Care: Treatment for Respiratory Exacerbations (respiratory illness)

Symptoms include increased cough, wheezing, secretions, congestion, and effort of breathing

4 times per day (to be used in addition to other chronic treatments)

- ☐ Chest physiotherapy (CPT) OR high-frequency chest wall oscillation (vest therapy)
- ☐ Insufflator-exsufflator (CoughAssist)
- ☐ Steroid nebs: budesonide (Pulmicort) or fluticasone (Flovent)

When symptoms worsen, do not improve within 2 days, or fever develops

- ☐ **Antibiotics** as ordered for 7 days, rotate those indicated
  - ☐ Clindamycin _____ mL (_____ mg/mL) G tube _____ times per day
  - ☐ Augmentin _____ mL (_____ mg/mL) G tube _____ times per day
  - ☐ Levofloxacin _____ mL (_____ mg/mL) G tube 1 time per day
  - ☐ Other _____
    (azithromycin and other macrolides may provide anti-inflammatory benefit)
- ☐ **Prednisone** (oral steroid burst) as ordered for 5 days (consider including with third or fourth exacerbation)
  - ☐ Prednisone _____ mL (_____ mg/mL) G tube _____ times per day
    1–2 mg/kg/day divided twice per day
    (maximum 60 mg/day; 5 mg/5 mL or 5 mg/1 mL)

Treatment for Comfort

Features suggesting uncomfortable breathing: distressed or anxious look on face, facial grimacing, appearing restless, tears, or becoming withdrawn

- ☐ **Fan to face** (decreases sensation of uncomfortable breathing)

Figure 6.4. A plan for home respiratory care. *Abbreviations:* GT, G tube; nebs, nebulizer treatments; PO, oral; SL, sublingual.

☐ **Morphine sulfate** _____ mL (_____ mg/ml) PO/SL/GT every ___ hrs as needed (prn)
0.05 to 0.1 mg/kg (max starting dose 5 mg) SL/G-tube every 3 to 4 hrs as needed (10 mg/5 mL, 20 mg/l mL), starting dose is 25%–30% of the dose used for pain, call for instructions to increase if seeing no benefit, be careful that the amount of the liquid concentration being used (mL) is the same as the intended dose (mg)

☐ **Midazolam** _____ mL (_____ mg/mL) PO/SL/GT every ___ hrs as needed (prn)
0.1 to 0.2 mg/kg G-tube/SL, max. starting dose 5 mg (2 mg/mL)

☐ **Glycopyrrolate (Robinul), hyoscyamine, atropine, or scopalamine**
for secretion management

Chronic and Acute Respiratory Treatment and Symptom Management

- Contributing factors to chronic and acute respiratory problems in neurologically impaired children:
  - — Ineffective cough with poor clearance of oral secretions
  - — Decreased effort of breathing from limited activity or muscle weakness: *hypoventilation*
  - — Chronic aspiration of oral secretions resulting in inflammation and infection: *pneumonia*
  - — Development of mucus plugs and volume loss (atelectasis): *ventilation/perfusion (V/Q) mismatch*
- Recurrent acute respiratory illness in children with neurological impairment who are known to aspirate, often called aspiration pneumonia, is a result of these contributing factors
- Treatment goals: though we cannot "fix" these contributing factors, we can use chronic and acute interventions to minimize the effects of these factors, maximize maintenance of health, maximize recovery when there is an acute illness, minimize symptoms, and maximize the best quality of life
- When considering procedures and surgical interventions for improving respiratory health (such as Nissen fundoplication, spinal surgery, and tracheotomy): Will the intervention treat a single cause of respiratory symptoms or are there other contributing problems that will not be altered by the intervention?
- Parents often worry about comfort/quality of life and can use this as a goal to guide decisions:
  - — What are the benefits and harms of the intervention available?
  - — Will the intervention improve my child's level of comfort?
  - — How much of each day is my child able to enjoy now compared to 6 or 12 months ago?
  - — Will interventions prolong suffering if there is further decline and less recovery to baseline?
  - — How will I know when I am doing **to** versus **for** my child?
- Morphine sulfate is safe and beneficial for alleviating respiratory distress
- Morphine sulfate can be used with other interventions or alone to meet the goal of comfort
- If symptoms become worse, illnesses more frequent, or time between exacerbations decreases:
  - — This does not reflect on the quality of home care but is due to the progression of the underlying disease
  - — Goals and plans can be reviewed if acute interventions no longer provide benefit for exacerbations
- Goals and hopes sometimes shift from treatment for recovery to care to maintain comfort
- **You are not responsible for your child's outcome; your child's medical condition is responsible**

Definitions

- *Hypoventilation*: Shallow breathing with reduced amount of air entering the lungs resulting in decreased oxygen and increased carbon dioxide in the blood
- *Pneumonia*: An acute or chronic disease marked by inflammation of the lungs due to infection and physical and chemical irritants, such as aspiration of oral secretions
- *V/Q mismatch*: A mismatch or imbalance in the areas of the lung available for exchange of oxygen and carbon dioxide between the lungs and the blood vessels

The antibiotics indicated in the "Respiratory Home Management" plan are based on the evidence for treating respiratory exacerbations that occur at home as a result of chronic aspiration. Morphine sulfate is also included, a reminder to consider the role of respiratory symptom treatment during acute respiratory exacerbations, with initial dosing recommendations provided. The plan also includes other information reviewed in this chapter. The cases of Derick and Nathan highlight the process of introducing the option of a home care plan to families.

The option of maintaining care in the home requires detailed home care plans that anticipate distressing symptoms and potential emergencies. Healthcare teams can attend to symptoms by creating more detailed and tailored care plans that utilize parental input, such as this example for a child (weight 20 kg) who has SNI and progressive respiratory failure (recognizing that each care plan must be tailored to the specific needs and goals of each child):

1. The following symptoms have been identified as indicating respiratory distress: increased heart rate, working harder to breathe (with increased use of chest muscles), "distressed" look on the face (often noted with facial grimacing), and increased secretions.
2. When these symptoms are noted, give 0.1 mL (2 mg) of morphine sulfate, by syringe, between the cheek and gum.
3. Vent the gastrostomy tube if there is abdominal distension, gagging, or vomiting.
4. If no improvement occurs within 30 minutes (by which time onset of action is expected), repeat the same dose of morphine sulfate.
5. If no improvement occurs in 15 minutes, give midazolam, 1 mL (2 mg), oral or by G tube.
6. For increasing secretions, give 8 drops of hyoscyamine, as often as every 4 hours.
7. Withhold feedings until distress remains resolved for 4 to 6 hours.
8. Call with any concerns: [phone number] during clinic hours, or [phone number] after hours, and ask for the physician on call for the Complex Care team [insert team name].

Strong cough versus weak cough

There are differences among (1) children who have a noticeable cough, even if the cough is less than effective; (2) children who have severe hypotonia, with shallow breathing and limited cough; and (3) children who

have no protective gag reflex or cough. Children able to generate sufficient force to produce sound with coughing and with the effort of breathing will typically have a noticeable increase in symptoms at the start of a respiratory exacerbation. Such symptoms can include increasing cough, "noisier" breathing, sounding more congested, and working harder to breathe. This observable information allows a family to anticipate a progression that will exceed the ability of routine chronic home interventions to minimize and creates an opportunity to initiate a home care plan as outlined in "Respiratory Home Management" (figure 6.4).

In contrast, children who are unable to generate much force with coughing and the effort of breathing may be much more "silent" when they have a respiratory illness and decline, as a result of insufficient force to generate recognizable symptoms. Observable information may be limited to an increase in respiratory rate and nasal flaring, without much cough or congestion. Such children are at risk for more "unexpected" declines in respiratory function. These children and their families will benefit from planning and preparing for such events, knowing how goals will guide decisions at such times. Parents and other caregivers can describe their child's ability to generate symptoms such as cough, the force of any coughing, how much mucus is mobilized during a cough, and any sound production with congestion, to understand how a respiratory event is likely to affect their child.

ACUTE RESPIRATORY DECLINE AND POTENTIAL FAILURE

One of the most frightening experiences for the families of children who have SNI is watching their child struggle to breathe with each illness and worrying that the child may die as the result of an acute respiratory exacerbation. Such stress may be experienced as a family lives through the child's recurrent respiratory illnesses or when the child is hospitalized and intubated for the first time. Even the first hospitalization for a respiratory illness that the medical team considers "routine" and not life threatening can be frightening: "I was told that children die from aspiration pneumonia. Does this mean my child may be dying?"

One of the goals of this chapter is to help families and healthcare teams anticipate such events and prepare for the decisions that parents encounter at such times. An essential part of preparing is to understand care plan options and how the different options can meet different goals. As families worry about health decline and physical suffering in their child, they often simultaneously "hope and prepare," as illustrated in figure 6.3.

Anticipating respiratory failure

The term *respiratory failure* is used in medicine to describe inadequate gas exchange by the respiratory system, with the result that the blood oxygen and/or carbon dioxide levels cannot be maintained within the normal ranges necessary to support life and avoid complications. A drop in blood oxygen is known as hypoxemia, and a rise in blood carbon dioxide is known as hypercapnia. Respiratory failure can occur both acutely and chronically, as happens in some children who have SNI and an increasing frequency of respiratory exacerbations.

The goal of medicine is to be proactive, to intervene before respiratory failure becomes respiratory arrest, with the resulting cessation of breathing. In the hospital, children are monitored to ensure that interventions, such as intubation of the trachea, can be used to avoid respiratory arrest. *Intubation* refers to placement of a flexible plastic tube into the trachea to maintain an open airway and to facilitate ventilation of the lungs, including the use of mechanical ventilation (respirator). The goal is also to identify when intubation is not consistent with the goals of care identified for the child, and to put steps in place to protect this child. This process is reviewed in greater detail in chapter 9.

Proactively identifying children at greatest risk and monitoring children with anticipated future risk

Children with the greatest risk for respiratory failure earlier in life are those with the greatest impairment of the mechanisms necessary for adequate breathing, including lack of a cough, lack of a protective gag response, and severe disordered breathing due to impairment of the centers in the brain that regulate breathing. As reviewed earlier, such children are at greatest risk for acute respiratory decline and failure without "warning." They also receive less benefit from the available treatments that minimize decline in respiratory function and maximize recovery during an acute illness.

When possible, anticipating and preparing for such an event allows families to consider and better understand the different care plan options for their child. Unfortunately, too often, these discussions take place only after a child has been intubated for the management of respiratory failure (Sritippayawan et al. 2003). Such discussion is usually delayed out of fear that it will be too distressing for the family. Fortunately, the literature is helping us understand that families find such discussions helpful and that

they do not lessen parents' hope (Mack et al. 2006, 2007; Wolfe et al. 2000). In the light of this growing evidence, it is important that families be empowered with information and that healthcare teams understand the hopes, goals, and values that will guide a family's decisions. Even when such discussions do not result in a decision, they do help prepare families for decisions during later events, as illustrated by the case of Kaitlyn (see "Case examples"). For these reasons, children and their families deserve the opportunity for the families to have appropriate and meaningful discussions in anticipation of acute respiratory decline.

More commonly, children with SNI initially have mild respiratory illnesses and increasing chronic symptoms such as congestion. This more gradual increase in symptoms and acute respiratory exacerbations can take place over years, before a child experiences an acute risk of respiratory failure.

It is helpful to consider such children on a continuum of risk, when considering and preparing for potential respiratory failure, rather than taking a watchful approach and monitoring each acute respiratory exacerbation. Given the inability to predict with accuracy when a future respiratory exacerbation might result in respiratory failure, families will benefit from being able to anticipate and prepare for such events. Yet it is equally important that families should not feel forced to engage in these discussions. Instead, opportunities for discussion need to be created.

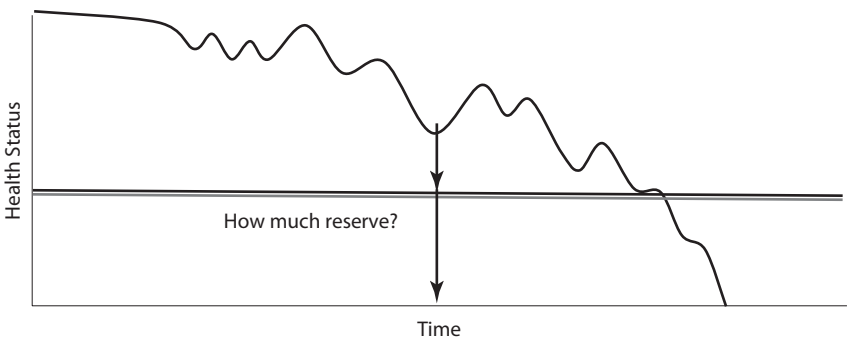
A family may find it useful to view this as a time to receive and consider information, without the need for a decision. It can also be helpful to identify someone such as a social worker or chaplain to assist with reflecting on what is important to the family in making any decision. In response to considering their child's risk for a future life-threatening event, one family said, "You don't need to prepare for joy but we wouldn't want to be unprepared for the worst." The goal is to ensure that families have the opportunity to think through "What if?"—meaning that some families will be preparing for an event that does not occur, or occurs much later, which in many ways is another example of hoping and preparing.

In considering this continuum of risk, parents can reflect on how much decline from their child's best health baseline they have observed. This is not intended as information for prognosis but rather as a way for a family to reflect on their child's history and anticipate the likelihood of respiratory failure. Depending on the child's health trajectory, this reflection can often help a parent understand the need to start planning for future events and reviewing information about different approaches and care plans, including associated decision making.

In these discussions, a useful goal is being informed and asking questions, without expecting any specific decision. Planning for an event can feel different from directly experiencing such an event. A few families have referred to this experience as feeling like a "dress rehearsal" that allows a better understanding of what to expect and helps identify further details to discuss for planning.

A final area for recognition is the intensity of the care provider role and how this can naturally result in parents and caregivers feeling responsible when a child's health declines. Parents and other caregivers deserve to be reminded that a decline in respiratory health in a child who has SNI is a result of problems caused by the impaired nervous system, not by insufficient care. This is a time to reflect on how the problems "are greater than the remarkable and loving care provided." Parents benefit from sharing their worries, reviewing their goals for their child, and being reassured that they are not responsible for the outcome.

Figure 6.5 provides a visual schematic for (1) identifying children at earlier risk for respiratory failure and (2) reflecting on a child's health trajectory, so as to anticipate an increasing risk of respiratory failure. This schematic can also be part of a process of reflecting on the potential ben-



How much reserve? Children at risk for respiratory failure with first respiratory illness:
- No discernible cough
- No gag reflex
- Severe hypotonia with diminished respiratory expansion of the lungs
- Disordered breathing of central origin with prolonged pauses in breathing

Parental reflection on their child's health trajectory: increasing risk for respiratory failure:
- How does your child's health this month compare with 6 months, 2 years, or 5 years ago?
- How much would you estimate that it has declined? None, by 25%, 50%, >50%?
- How much daily pulmonary treatment is needed to maintain the current level of health?
- How often in a month is your child sick now compared to then?
- How much does your child enjoy each day now compared with then?
- How often is your child uncomfortable during a week now compared with then?

Figure 6.5. Anticipating risk of respiratory failure

efit and harm of a surgical intervention, intubation for respiratory failure, or the ongoing use of acute care plans that treat infection and inflammation.

Acute respiratory care in the hospital and in the home

When a child who has SNI experiences his or her first respiratory illness, the focus is on finding out what is contributing to the decline in respiratory health, as reviewed earlier in this chapter. Chronic interventions and treatment for acute respiratory exacerbations are typically beneficial, often for years to decades.

Reviewing the benefits and risks of respiratory treatment plans becomes more relevant when a child is experiencing more frequent respiratory exacerbations or is receiving decreasing benefit from the acute interventions used during respiratory exacerbations. This is a time to review the question "Is there more we can do?" while families and medical care teams reflect honestly about hopes, worries, benefits, and burdens. This process will assist with the goal to minimize the use of interventions that are less likely to provide benefit but are sometimes pursued out of a sense of needing to "do something." This is also a time to review the interventions available for treating the discomfort of respiratory distress, in anticipation of the next respiratory exacerbation.

Questions about benefit and harm can include the location of care. Care in the hospital can provide significant benefit, but some families find that the benefit decreases over time. Though not often considered, it can be helpful to reflect on how this benefit can change for some children with chronic conditions.

In general, care in the hospital provides treatments that cannot be initiated in the home (IV medications), monitoring for respiratory failure (for children who have no restrictions on resuscitation and use of mechanical ventilation), and respite for the family from the effort of around-the-clock care. By thinking about what can be done in the hospital, a family can also determine when this location of care no longer meets the goals they have identified.

It is also useful to recognize the uncertainty of benefit of some care plans over others. As an example, for a child who has SNI and recurrent respiratory exacerbations, whether there is greater benefit from the use of IV antibiotics initiated in the hospital over antibiotics initiated as part of a home care plan is not always clear. The risks include hospital-acquired bacteria and bacterial resistance with the repeated use of broad-spectrum

IV antibiotics; risks can then be considered within the context of the benefit that the hospital can provide. In addition, there may be some advantage for a care plan that can be initiated sooner in the home, rather than waiting for the child to be evaluated in the clinic or hospital before a treatment plan can be initiated.

The benefits and limits of the expertise available in the hospital must also be considered. As an example, more hospitals are utilizing the expertise of hospitalists—that is, hospital-based general physicians. The hospital also provides access to other specialists to assist with care, as needed. The strength of the hospitalist is the ability to provide exceptional hospital-based care. However, the hospitalist may have less experience with what the care of such children looks like in the community, which may be reflected in hospital-based care overemphasizing the child's risk, with the focus on anticipating and intervening before respiratory failure occurs and thus erring on the side of caution. There may also be an overemphasis on tests and on the benefit of treatment in the hospital. These statements are not intended as a criticism but rather as a reflection on the strengths and limits of care in the hospital for children who have chronic conditions, factors that are typically not considered.

When considering the role of the hospital and home care settings, we should keep in mind that children who have SNI and recurrent respiratory exacerbations often do better than expected. Though this outcome has not been studied, physicians caring for this group of children are hard pressed to recall cases of children who died in the community as a result of unexpected respiratory failure (with the exception of children who do not generate observable symptoms). The deaths that do occur in the community seem to be, most commonly, a planned event or, less commonly, an unwitnessed event during sleep.

This is not intended to downplay the risk of respiratory failure in such children but to recognize the uncertainty that often has a better outcome than is suggested by the worries of medical teams. Again, these worries may represent the need to err on the side of avoiding an unanticipated crisis, resulting in an overemphasis on the benefits and under-recognition of the risks of the hospital, and an under-recognition of the utility of home care plans that can provide benefit and symptom relief for children who have SNI, often for years. Most important, though, such worries are opportunities for families and medical teams to engage in discussions that help the family clarify their hopes, values, goals, and worries. Ideally, those providing information will impart as little bias as possible when reflecting on the care plan options. An important reminder here, when con-

sidering the risk of respiratory failure: the exception is those children who do not have observable symptoms and are at greater risk for acute respiratory failure, such as children with no gag reflex, minimal or no cough, severe hypotonia, and disordered breathing of central origin.

Effective and safe home care plans require a knowledge of the availability of local systems that can assist with and support delivery of the care plan in the home, including ready access to a healthcare team that knows the care plans for the child and is available 24/7 to attend to concerns and questions as they arise. We should also note that a home care plan and hospitalization are not mutually exclusive. The option of hospitalization always exists if the child's health worsens despite initiation of a home care plan. Each family must also be reassured that plans can change as the child's needs change. As an example, for a family that has experienced decreasing benefit from hospital-based care, a goal may be to focus on home treatment plans with no further hospitalizations. Yet they may later request a hospitalization if they feel that the plans and support in place are not meeting other goals—for example, if their child has persistent discomfort and distress.

Clearly, the hospital is an important option for location of care for children who have SNI. The intent of reflecting on the home versus the hospital is to ensure that both are given equal consideration (table 6.8).

In this era of medicine, it is essential to consider how chronic care differs from acute care and to make sure that families are supported in defining the goals of care that will guide decisions for their child. In this process, families should have the necessary information while being assisted with identifying their hopes, goals, and fears for their child. Such discussions can then support the plan that is best suited to the family's goals and values and will avoid focusing solely on what can be done medically. Ideally, this process recognizes the need for parents to be a "good parent," avoids creating a sense of "doing nothing," and avoids an assumption that the only option is to bring the child into the clinic and hospital for each illness.

Use of mechanical respiratory support

Mechanical respiratory support should be anticipated and discussed in advance of an acute need. Any discussion ought to consider the other areas of care reviewed throughout this book, including attention to symptom management, focusing on the process of decision making rather than the decision to be made, and understanding the key components of

TABLE 6.8 Home versus hospital

	Benefit	Burden or harm
Home	• Earlier initiation of acute treatment with home protocols (figure 6.4) • Avoids invasive testing and IV placement • Familiar setting for the child • Less disruptive	• Caregiver fatigue • "I'm not a doctor" • "Could we have done more?" • Challenge of identifying respiratory decline that may result in respiratory failure (for children with no restrictions on resuscitation)
Hospital	• More frequent airway clearance • Allows monitoring for respiratory failure (when care plan includes the use of mechanical ventilation if needed) • IV antibiotic options for broader coverage • Short-term use of noninvasive ventilation	• Disruptive • Family not feeling in "control" of care plans; their expertise sometimes dismissed • Frequent use of invasive tests and procedures (blood tests, IV placement, etc.) • Infection by antibiotic-resistant bacteria, hospital-acquired and a result of broad-spectrum IV antibiotics

decision making. Chapter 9 covers these components in greater detail. A few points are reviewed here.

Mechanical support can involve noninvasive positive pressure ventilation (NIPPV), such as continuous positive airway pressure (CPAP) and bi-level positive airway pressure (BiPAP); invasive ventilation with intubation for acute use of mechanical ventilation or placement of a tracheostomy tube for chronic use of ventilation; and the use of a bag valve mask (Ambu bag) for a person with a tracheostomy tube, to intermittently expand the lungs.

Decisions will fall into two types: acute use of mechanical support and chronic use of mechanical interventions. There is limited information on outcomes following short-term use of ventilation for respiratory failure in children who have SNI. One study retrospectively reviewed all children with neurological impairment who were intubated for respiratory failure, with a review of the outcomes over one year (van Gestel et al. 2010). For the 22 children with SNI, the average duration of mechanical ventilation was 16 days (range 3 to 34 days). Of these 22 children, 11 died and 6 had a one-year survival with no events and no further hospitalizations. Eight of

the deaths occurred at home, following a decision by the family not to readmit their child with any future respiratory illness. Overall, the children with SNI in this study had repeated, prolonged, and complicated admissions to the ICU. In contrast, the children with moderate impairment had significantly fewer deaths and readmissions to the ICU for intubation.

When reviewing the acute use of intubation and mechanical support, it is beneficial to discuss the emotional aspects and the ethics of not using an intervention versus initiating and later discontinuing that intervention. Though these two actions can feel, emotionally, very different, they are ethically the same. With this information, one family may decide to use intubation and mechanical support of breathing, and then address later any decision about continuing use of the mechanical support if there is not sufficient recovery. Another family may view using such technology as prolonging the inevitable: "Even if he recovers the first time that his breathing fails, it will just eventually happen again. We want to focus on all of the other things we can do, but not put him through unnecessary discomfort or the uncertainty of recovering enough to get off the ventilator."

Chronic use of mechanical respiratory support involves similar decisions, including discontinuing such support if it is no longer meeting the goals identified for the child or is resulting in prolonged suffering. It is even more critical when considering the use of home ventilation that a family should have a realistic picture of the resources in the community to support such a plan. The cases of Derick, Kaitlyn, Samantha, and Jonathan (see "Case examples") highlight some of these decisions.

Goals that are used to guide decisions may include maintaining comfort, maintaining health for an upcoming family event, or maintaining health without the use of invasive interventions. Other goals may reflect the site of care for a child, if an intervention, such as a tracheostomy or chronic ventilation, would require transferring the child to a new location. In this scenario, families should be supported in any decision. If the family believes that their child is "happy and comfortable" in his or her current location of care, they may feel that the loss of the child's familiar environment and caregivers would be a greater burden than the potential benefit of the intervention. If the focus is solely on the medical decision, a family may feel they "don't have a choice" or that they are being "bad parents" if they consider not using the intervention. By identifying and remaining focused on goals as a guide to such decisions, families can view their decisions as being informed by knowing which interventions will or will not meet such goals.

Consideration of acute mechanical support also involves decisions about the benefit and harm of resuscitation. Several details are important for children who have SNI:

- These children have a significant risk for rib fractures during chest compressions, given that many of them have osteoporosis because they are nonambulatory throughout life. The harm from chest compressions should be considered and could outweigh any potential benefit.
- Most children who have SNI experience cardiac arrest (the heart stops) as a result of respiratory arrest (breathing stops), excluding children with such conditions as congenital syndromes with associated cardiac defects. When breathing fails, the lack of oxygen results in failure of the heart. When a decision is made not to intubate a child during respiratory failure, a family can be informed of the lack of benefit of such interventions as chest compressions, cardioversion (electric shock to the heart), and IV medications for the heart. For the family, this information can prevent their feeling responsible for each decision from a "laundry list" of interventions by focusing on the primary cause of failure (respiratory failure), and it can minimize the use of potentially harmful interventions with no benefit.
- Some hospital forms include interventions beyond intubation that are used for managing acute respiratory illness, such as nasal or oral airway and positive airway pressure ventilation (CPAP/BiPAP). Though these interventions are less invasive, decision making is similar: what is the potential benefit to health, and how will the process meet any identified goals of care, such as maintaining comfort? In addition, any intervention can be discontinued if it is no longer providing benefit or is prolonging suffering.
- It is helpful to consider the benefit and burden of CPAP/BiPAP in a similar way to the discussion of intubation, such as acute versus chronic use.

Many hospital-based resuscitation order forms now include advance care planning for other medical interventions. Completing these forms can serve as a prompt to review interventions beyond intubation and cardiac resuscitation. This subject, including definitions of the terms commonly used, is covered in greater detail in chapter 9.

Finally, parents should be prepared for the possibility of being asked about prior decisions, as they encounter "well-intended" new healthcare

providers. Questions can focus on decisions to do something as well as not to do something. Families should be helped to prepare for how they wish to respond. They might say, for example, "This has been discussed and documented. You are welcome to contact Dr. X to understand our prior discussions and care plans." The family can be provided with comprehensive documentation and relevant forms to be shared when needed.

SUMMARY OF DECISION MAKING FOR CHILDREN WHO HAVE SNI: DECLINING BASELINE HEALTH AND DECREASING BENEFIT FROM ACUTE TREATMENT OF RESPIRATORY EXACERBATIONS

- When care plans and decisions are being considered, parents benefit from an opportunity to reflect on, share, and celebrate stories about their child's life.
- Rather than focusing on the inherent issues of uncertainty, caregivers can use a schematic for anticipating risk and outcome (figures 6.3 and 6.5):
  - — Identifying children at risk for respiratory failure
  - — Assisting parents in reflecting on their child's decline in health and decreasing benefit from acute and chronic treatment, thus facilitating reflection on the benefit and harm of acute treatment and surgical interventions: "When are we doing *to* versus doing *for* my child?"
  - — Use of the case illustrations and discussions in this chapter to empower the expertise of parents and other caregivers who see the child every day
  - — Use of expert information from parents to help medical teams better understand the potential benefit and harm of an intervention based on the child's health trajectory
- Decisions about surgical interventions must (1) factor in what the intervention can "fix," (2) acknowledge other possible contributing factors that the intervention will not alter, and (3) consider the interventions in the broader context of the child's health trajectory.
- Ideally, decisions about intubation and mechanical ventilation are anticipated. Information and recommendations can be considered, without expecting a decision to be made.
- Decision making involves more than the medical facts; it also involves the values, hopes, goals, and worries of the family.

- When identifying and clarifying information, parents benefit from a team that attends to the emotional and spiritual needs of the family, including siblings, and recruits the expertise of social workers, chaplains, and child life specialists, for example.
- Fears can shift, such as from the worry that a child will not recover, despite treatment, to the worry that the child's suffering will be prolonged with continued treatment.
- Hopes and goals can shift, such as from using treatment to maximize recovery of health to using care plans to maintain comfort.
- Fundamental is a parent's desire to be a "good parent."
- Parents benefit when their hopes are supported rather than viewed as an "unrealistic" view of their child's future (Feudtner et al. 2010).
- Distressing symptoms must be identified, managed, and anticipated; the child's suffering must be minimized.
  - — Management of distressing symptoms requires expertise; this can be provided by a palliative medicine specialist, for example.
  - — Without symptom management expertise, there is often an overemphasis on the risk of symptom management, which can leave families believing they need to choose between life-sustaining treatment or "comfort care" until their child dies.
  - — Symptom treatment for dyspnea can be incorporated into medical treatment plans for acute respiratory exacerbations, as outlined in figure 6.4.
  - — Addressing dyspnea can lessen decisions to use an intervention out of the fear that the child will suffer without the intervention.
- Families should have the opportunity to reflect on the benefits and burdens of care plans in the hospital and the home; this is an important consideration for all chronic conditions.

CASE EXAMPLES

The following cases illustrate information in this chapter. Note that each case involved interdisciplinary support such as a social worker, chaplain, or child life specialist for sibling support, along with various medical specialists.

Decision making about tracheotomy and symptom management

Sofia is a 4-month-old twin born prematurely, with a corrected gestational age of 2 months. She suffered an injury to her brain as a result of a twin-twin

transfusion; her head MRI showed severe cerebral loss. Her parents have concerns about her breathing. A sleep study is obtained and identifies severe obstructive apnea. As there is no anatomical cause of obstruction, this is thought to be secondary to her abnormal tone.

Given the severity of the findings in the sleep study, the specialist plans to share with Sofia's parents that "they either need to admit her today and schedule a tracheotomy or make her DNI/DNR" (do not intubate/do not resuscitate). Following a broader discussion between the sleep specialist, otolaryngologist, neurologist, and palliative medicine specialist, information and options are presented to Sofia's parents.

Following the medical team's lengthy discussion with the parents, they identify their hopes, worries, and goals for Sofia. They are concerned about her comfort. Their goals for her are improved comfort, improved sleep, and a "meaningful life." They worry that a tracheotomy will prolong her life without providing benefit for a meaningful life. They also hope she will do better than anticipated.

Their worries about Sofia's comfort include increasing irritability, with excessive crying daily and poor sleep. Features suggesting pain include moaning, inability to be consoled, and facial grimacing. Symptoms occur out of the blue, with intestinal gas, and prior to bowel movements. It is unclear whether the irritability reflects air hunger or is related to central pain. The parents focus on a plan to use interventions that will allow Sofia to be more comfortable, and they decline the option of a tracheotomy. They recognize the risks and continue to hope that Sofia will do well without the tracheotomy. In considering options, gabapentin is initiated and soon results in improved comfort and sleep. This corresponds with the parents noting a decline in the features that first raised their concerns about Sofia's breathing. They later choose not to repeat the sleep study, as this would not change their approach. They continue to focus on her level of comfort and how well she appears to be doing. Sofia continues to do well 3 years later. She is described as very happy and sociable. The overall speculation is that pain contributed to changes in muscle tone, which resulted in a significant change in her airway.

Key points

1. Decisions about a tracheotomy should factor in the hopes, fears, and goals of the parents, which are as important as the medical details. Parents can be assisted in identifying their hopes, fears, and goals and in understanding how these factors have a place in decision making.

2. When discomfort and pain are identified, they should be given equal consideration without unduly influencing parents to feel that they are choosing between allowing their child to live or allowing their child to be comfortable.
3. Though this topic has not been studied, this case raises questions about the role of pain in airway tone in children who have SNI—especially infants with the smallest airways—just as pain can alter muscle tone throughout the body.

Decision making about spinal surgery

Jenay is a 7-year-old girl who has a chromosomal disorder and various medical problems, including GER, reactive airway disease, an immune deficiency managed with monthly intravenous immune globulin (IVIG), and severe NM scoliosis. At birth, Jenay was expected to die early in life and was discharged to her home with hospice support. Given how well Jenay has done, her parents now approach her life as "taking each illness as it comes." Jenay was referred to palliative care by her orthopedic surgeon, so as to assist her parents with decision making about spinal surgery for her NM scoliosis. In addition, she is assessed to need placement of a feeding tube if surgery is pursued, given her current rate of weight gain.

Throughout the discussion, Jenay's parents articulate that their greatest worry is that surgery will adversely affect her current quality of life. Jenay is described as being happiest when she is on the floor with her toys and her puppy, and with the family. The parents share the experience of Jenay's previously being in a body cast and unable to play in the way she enjoys. Jenay would cry because of the position she was in and was much more likely to fall in an unprotected way. They also describe their worry that Jenay, with surgery, will not sleep as well, because she sleeps best when she is in a curled position. "She has slowly adjusted to the changes in her spine. A sudden change may be too difficult for her to adjust to." They also say, "It's not going to make her normal and not help her walk, but it may impact what she enjoys. We don't want to take away her enjoyment and we want her to be comfortable."

Jenay's parents understand that without surgery, Jenay's spine will "deteriorate" and that she may die at an earlier age as a result of restrictive lung disease. "We don't want her to die, but we don't want her to live longer with suffering." They also indicate that their other goal for Jenay is to always live with her family, a goal that becomes difficult if she outlives their ability to care for her. They also factor in the need for placement of a feeding tube before

surgery. Her mother says that Jenay would pull at the tube. "She won't leave things alone. She is so innocent and we can't explain things to her to help her understand." "She is a little bundle of trouble and as sweet as pie."

After a lengthy discussion, Jenay's parents believe that surgery would have a greater potential for harm for Jenay in terms of how she enjoys her days than the intended benefit of the surgery. They recognize that this risk is an unknown, but feel they can't take that risk for Jenay. A plan is made, in discussion with Jenay's surgeon, that 6 months is a "reasonable" time for follow-up, a period that will still allow the option of surgery. The parents agree that this period will allow them to reflect further on the discussion and then return to revisit their decision. The plan includes obtaining a follow-up spinal X-ray at that time. At the follow-up, there is no significant progression of the severe scoliosis. Jenay's parents remain committed to their original decision, after an opportunity to revisit the risks and burdens of surgery that they have identified for their daughter.

Key points

1. Decision making is a process that ideally combines medical facts and the anticipated impact of interventions on a person's quality of life. Because it is impossible to know with certainty what the outcome will be, making a decision often involves determining which goals and worries are most important, then allowing those to guide the decision. In Jenay's case, whether the parents' greatest worry would come to pass was unknown, but it was too great a risk to take, given the negative effect on Jenay's ability to enjoy each day. This decision, as described in chapter 9, is a decision to "avoid potential harm."
2. Parents are not choosing to let their child die earlier; they are choosing how to ensure the best life possible for their child. They can be supported if this information is framed to minimize the associated guilt about what it means to be a "good parent."
3. Parents want their child to live as long as possible and then, as their child gets older, they may start to worry about who will care for their child when they are not able to do so. Though this worry can feel conflicting for a family, it is beneficial to recognize that it becomes a concern for many families. This future reality is appropriately factored into current decisions, just as other quality-of-life issues are considered.

Decision making about Nissen fundoplication

Danny is a 10-year-old who has SNI as a result of traumatic brain injury as a child. He has been experiencing an increasing frequency of vomiting and respiratory illnesses. His medical team has indicated that he "needs" another Nissen fundoplication to manage these problems. Danny's mother is uncertain about putting him through another surgery but wants to give him a chance for improvement.

A discussion identifies the mother's goals for Danny. She wishes to see Danny's comfort improve and she worries that, without the surgery, it will only get worse. Questions as outlined in figure 6.5 are asked, as a guide to Danny's health trajectory. It is identified that Danny is sick almost monthly, often resulting in hospitalization. His health has declined by 50% to 75%. He has fewer "good" days and typically is uncomfortable for part of each day, averaging 30% to 40% of each day.

In reviewing Danny's history, it is apparent that he has had many prior interventions, comprehensive evaluation of ongoing problems, and exceptional chronic care. There is a discussion of the factors contributing to his current respiratory problems, with acknowledgment of the many problems that cannot be "fixed." In thinking about how much Danny's health has declined, his mother cannot imagine that this intervention could provide sufficient recovery. Care plans that can address Danny's discomfort from vomiting and respiratory symptoms are reviewed in detail. With this information, the shared decision of Danny's mother and the medical team is to focus on the things that can improve Danny's comfort and to not pursue surgery, given the risk of retching and pain that can occur in some children following fundoplication. Danny's mother is relieved. When she was first considering surgery, she "didn't know what to do."

Key point

1. As with Jenay, the risk of increasing Danny's physical suffering, in this case as a result of increased retching following Nissen surgery, is greater than the potential health benefit proposed by the medical team.

Recurrent respiratory exacerbations, home care plans, decisions about resuscitation, and dyspnea management

Derick is a 22-year-old who has cerebral palsy and intellectual disability, resulting in his being nonambulatory and nonverbal. He receives fluid and nutri-

tion by a G tube. Other associated problems include a history of a fracture, NM scoliosis, and recurrent pulmonary illnesses. He has experienced an increased frequency of respiratory exacerbations over the years, now every 2 to 3 months. His chronic care includes nebulizer treatments, with a daily inhaled steroid and as-needed albuterol and Atrovent; chest PT and pulmonary vest for secretion mobilization; suctioning as needed; and home oxygen as needed. A sleep study identified mild obstructive apnea. BiPAP has been used at home: "Even though they say he needs it, we don't use it because it makes him mad." It is noted that "he might benefit from a tracheotomy."

With the increasing frequency of respiratory exacerbations and hospitalizations, and the decision to be made about a tracheotomy, a discussion takes place to better understand the family's hopes, fears, and goals. His parents describe Derick's days as enjoyable between respiratory illnesses. They are not ready to "give up on him." They share their worry that the hospitalizations are providing less benefit and are distressing for Derick. One of his home care nurses worries that there will be criticism if something happens to Derick at home. Overall, his parents estimate that his health has declined by more than 50% over the years. The discussion also reveals that he appears to be in significant distress during acute exacerbations.

To assist with addressing these goals and worries, a home care treatment plan for future respiratory exacerbations is reviewed. Strategies for symptom management are discussed in detail. This discussion acknowledges the goal to continue to use chronic and acute interventions for as long as they provide benefit, including recovery from acute respiratory illnesses. The potential benefit from a tracheotomy is discussed in the context of Derick's declining health and the multiple contributing factors that would not be altered by this intervention.

The parents continue to hope for as many good days as possible and believe that this home care plan will help meet that goal and avoid distress from hospitalizations. They are interested in including in the care plan interventions that can lessen discomfort. They had feared that "when the time came" they would "need" to have Derick intubated so that he would not have to "suffocate" to death. They also say that "we couldn't think beyond that point, we didn't know what else we could do."

This discussion then leads to information about the use of resuscitation at home or in the hospital. The discussion does not involve asking "Do you want Derick intubated?" but rather how such an intervention would fit within the other goals and worries identified. Scenarios discussed include intubation with hospitalization and mechanical ventilation (use of a respirator) and possible outcomes: the potential that Derick would recover; the potential that he would not recover, resulting in discussions to discontinue the mechanical

support if it was believed to be prolonging his suffering; and the inability to prevent future events if Derick did recover from a respiratory failure. The parents are also asked whether it would be okay to consider "What if?" including if Derick were to die, and what would be important to them at that time. They said that holding Derick, keeping him comfortable, and telling him they love him would be most important. To meet these goals, the parents are given permission to "protect" Derick from intubation if they feel it would result in a greater risk of unnecessary harm and prolonged suffering. They understand that this is intended as an opportunity to inform and reflect without expecting a decision.

At a follow-up discussion, Derick's parents share their goal to focus on maximizing his health and comfort for as long as possible at home. From this information, a recommendation is made to document "do not attempt resuscitation" to protect Derick, given the goal of no further hospitalizations. His family agrees to this recommendation; they say, "This is the hardest thing we have considered as a family. But in thinking what we want for Derick, it helped us identify what we don't want for him. We recognize we could have him intubated and he could possibly recover after mechanical ventilation. But we don't want to take the chance of that being his last experience and away from home."

Three months later, Derick's mother calls to share that they had given Derick morphine sulfate at the time of a new respiratory illness, along with initiating one of the rotating home antibiotics outlined in the home care plan. They did not use this intervention with the first exacerbation following the discussion of the home care protocol. She says, "It is the best he has looked in years. And he had no respiratory depression, just as you had said, though we still feared. We wish we had used morphine earlier." Two years later, Derick continues to have benefit from this home care plan.

Key points

1. Identifying and addressing dyspnea is an important part of decision making to ensure that decisions are not made out of fear of suffering.
2. Though outcomes have not been studied in this population, individuals often do better than expected, including with home care protocols such as that outlined in figure 6.4, and when distressing symptoms are managed.
3. A discussion of resuscitation should take place after an understanding has been reached of the family's hopes, fears, and goals for their child. The discussion should not involve asking "Do you want us to intubate?" but it should focus on how the outcome might look with and without the intervention, within the context of identified goals.

Alternative plans need to be offered so that a decision not to intubate does not feel like "giving up."

Discontinuing mechanical support thought to be prolonging suffering

Kaitlyn, a 6-month-old girl who has Aicardi syndrome and intractable epilepsy, is admitted to the hospital with decreased oral intake and dehydration. A chest X-ray (CXR) identifies a pulmonary infiltrate, consistent with pneumonia and/or atelectasis. A VSS confirms aspiration, including with thickened liquids. A G tube is placed to meet the following goals, identified in discussion with Kaitlyn's mother: prevent future episodes of dehydration, assist with nutrition, prevent aspiration from oral feedings, and provide comfort.

Kaitlyn's mother asks, "What can we expect her future to look like?" Conversations related to this question take place in the hospital and during outpatient follow-up visits. The care team includes a neurologist, chronic care specialist, social worker, and chaplain.

Kaitlyn is considered to be at high risk for sudden respiratory failure, based on the following information: minimal cough noted at home, despite identifying the infiltrate on CXR; lack of any cough during aspiration, as assessed at the time of the VSS; and severe hypotonia, including the inability to lift her head when prone. Discussions review this risk, as well as seeking out the worries, hopes, goals, and values of the mother. A balance is sought to provide opportunities to prepare for and discuss "What if?" without "forcing" the mother into any decisions she is not prepared to make. The role of home hospice is introduced and declined.

At 8 months of age, Kaitlyn is again hospitalized as a result of a persistent decrease in O_2 sats, despite home respiratory care plans that include oxygen. She is treated with IV antibiotics and chest PT. Conversations prior to and following this hospitalization involve options of care, including limiting invasive interventions such as intubation. Kaitlyn's mother feels that she "can't make such a decision" for her daughter. She remains "scared" and worries about her daughter's suffering and her lack of "meaningful" interaction with the environment.

At 10 months old, Kaitlyn is admitted to the hospital following a more significant decline in her O_2 sats, resulting in intubation in the emergency department before admission to the ICU. Both parents are present, with psychosocial support provided. Kaitlyn's mother's questions focus on the potential for Kaitlyn to recover from this event and the risk of future events. The parents consider their options and later ask to discontinue the mechanical ventilation.

The care plan is focused on the parents and other family members being present, holding Kaitlyn, and interventions to ensure her comfort. Following a process to wean ventilation and then remove the tube, Kaitlyn dies within 15 minutes, remaining comfortable while held by her mother.

Key points

1. Allowing a parent to anticipate and prepare does not always result in an "active" decision about what to do or not to do, yet the discussions can be beneficial for when a family experiences an event in "real time."
2. Such preparing allows a focus on identifying and attending to the physical, emotional, and spiritual needs of the child and family.
3. Continuity increases trust and allows more effective support as events unfold and decisions take place.

Prenatal consideration of intubation after birth

A meeting with a neonatologist is scheduled after parents have been informed that their fetus has a skeletal dysplasia that typically results in early death as a result of respiratory failure. They note that they are pregnant with a girl and have selected the name Samantha.

At the meeting with the neonatologist and a social worker, the parents are presented with all options, including intubation, to "see how things go." Following the meeting, the social worker spends more time with the parents, as they had remained quiet though attentive throughout the discussion led by the neonatologist. After some time, they open up with their worry that if their daughter is intubated, she most likely will remain ventilated rather than live without mechanical support. They feel like "horrible" parents for the thoughts they share: "We have three other children and we worry that it wouldn't be fair to them to have our daughter requiring so much care just to live. But even if we wanted her to come home with us on a ventilator, we live in a small town far away from any major city. How can we realistically expect such a care plan to work in such a remote setting?" The parents are reassured that these are appropriate and essential details to factor into such a difficult decision. The parents share how distressing this experience has been and how much they want an opportunity to hold their daughter.

There is recognition that such a goal can be supported and that this can include the decision to "protect" their daughter from interventions, such as

intubation, that would interfere with this goal. It is acknowledged that such a decision would also be consistent with the other worries that the family has shared.

The pediatric palliative team is consulted to assist with arranging a care plan for the family. This includes a plan for the delivery to occur in the local community, with support from the local hospice if Samantha survives to go home. A detailed care plan is developed and adjusted, based on communication with the local hospital and hospice. The pediatric palliative team remains available to support the care plan that has been developed.

Key points

1. Conversations with parents should combine sharing information with asking questions that allow the team to understand the parents' hopes, worries, and values, which need to be part of the decision-making process.
2. It can be beneficial to bring the parents' "voice" to the beginning of the discussion and then allow this voice to guide the order and framing of the medical information. "We are here to discuss your daughter's medical problem. It will help us to first know you better, what you understand about your daughter's medical problem, and then some of your hopes and worries. Let's start with you telling us a little bit about yourselves and your family and your understanding of your daughter's medical condition."
3. There is a risk of focusing solely on information about the medical "facts," and then turning to parents and asking, "What would you like us to do?" Ideally, parents are asked, early on, "Tell us about your family. What are your hopes for Samantha? What do you worry about, what do you find most important as you consider decisions?"

Decline in neurological function, decisions to discontinue home ventilation, and symptom management

Jonathan is a 14-year-old boy who has SNI as a result of birth asphyxia. His medical history includes a seizure disorder, use of a feeding tube for all fluids and nutrition, intrathecal baclofen pump, and a tracheostomy tube with home mechanical ventilation. He is being assessed following two hospitalizations in the past month as a result of changes in his level of alertness. He is difficult to arouse, has a decrease in heart rate to the 40s, and has a decrease in respiratory

effort, with O_2 sats in the mid- to high 90s. Assessment does not disclose any clear reasons for the changes observed.

These changes are new for Jonathan over the past 2 months. He has been sleeping more and has episodes of a lower heart rate, in the 40s, compared with his previous baseline in the 70s when sleeping. He is also noticed to have colder hands and feet over the past several months, and they can appear purple and puffy at times. These changes in his extremities do not correlate with his heart rate. One family member states, "This might be the reality of Jonathan's new baseline." The family also notes that Jonathan has "not been the same" since a family member involved in his daily care died, 11 months ago.

Discomfort is also identified as a concern. Most recently, Jonathan has developed persistent pain since a urinary tract infection 3 months ago. The pain appears to be localized to his abdomen and increases before a bowel movement and flatus. Jonathan has also been experiencing more feeding intolerance. All evaluations have produced negative findings, including blood and urine tests, abdominal CT scan, and head MRI, which is unchanged from a prior study. When uncomfortable, Jonathan develops a significant increase in clonus and muscle spasms.

A lengthy discussion identifies the hopes, worries, and goals of the family. In this discussion, there is consideration that the clinical changes in alertness, heart rate, respiratory effort, circulation, and discomfort may reflect a decline in the function of Jonathan's brain. It is acknowledged that no test can confirm this consideration. There is general agreement from all family members that this is probably the best explanation for the ongoing problems, given that all test results have been negative and that there is no improvement despite alterations in some of his sedating medications.

There is also discussion about the option to discontinue technology that has previously been beneficial but might later be viewed as prolonging suffering. This is approached as an opportunity to inform without expecting a decision. Hospice is offered and accepted as a resource to assist with the care plans in the home.

The initial plan focuses on Jonathan's comfort. Treatment includes gabapentin for central neuropathic pain as a potential contributing factor to his discomfort, and the use of an opioid, as needed, for pain or dyspnea. In addition, his total feedings are decreased by 25%. Over the next week Jonathan has significant improvement in his comfort, with longer periods of alertness and responsiveness. The family now believes that his clonus and muscle spasms, which had been treated with increasing doses of diazepam, are significantly improved with the new medications. Jonathan is described as looking the best he has looked in more than 3 months. The opioid dose is increased by

30% to 50% when needed to maintain his comfort. Jonathan is more comfortable as well as alert, with no alteration in his respiratory pattern.

The following week, he again develops prolonged episodes of unresponsiveness and changes in his extremities. As this persists, the family decides that "it is time" to discontinue his ventilation. This is framed as meeting their goal to not prolong any suffering for Jonathan. Arrangements are made to assist with this process, attend to ongoing symptom management needs, and provide emotional support for the family.

After ventilation is discontinued, Jonathan continues to be responsive to his family over the next 48 hours. Of note, his opioid dose at this time is 10 times the starting dose prescribed, yet he is awake and interactive at times. He dies 3 days after ventilation is discontinued, surrounded by his family as they celebrate his life. They feel that Jonathan remained comfortable throughout this time.

Key points

1. It is helpful for families to remember the previous benefit from technology, if they are now considering discontinuing that technology because of decreasing benefit or prolonged suffering.
2. Children who have SNI can undergo emotional changes. Jonathan appeared to suffer emotionally after the death of a family member who had had an important role in his daily life. In retrospect, Jonathan was viewed as "at times seeming to have lost the will to live" following this death.
3. Jonathan had a history of increasing clonus and muscle spasms that, in retrospect, were partly secondary to pain, such as central neuropathic pain. These problems later seemed to benefit more from pain treatment than from increasing baclofen and diazepam doses used earlier.
4. Because Jonathan's clinical changes had no clear explanation, based on information available from studies and interventions, they were thought to reflect a decline in function of critical areas of the brain. This factor is probably under-recognized, as it can be viewed as a potential explanation only after evaluating for possible causes. Changes that might be seen as resulting from ongoing decline in the brain, even in the setting of a "static" disorder, include intermittent apnea, decline in the level of alertness, increasing autonomic dysfunction (including alteration in the vascular tone of the extremities and changes in intestinal motility), and escalating pain features. Such changes can initially be intermittent, then become slowly progressive.

5. Given the fear over the use of opioids, it is worth reflecting on the benefit and lack of harm for Jonathan from the increase in dose. The initial dose was 50% of a dose used for pain, accounting for Jonathan's fluctuating alertness. This dose was then titrated in a standard manner, increasing by 30% to 50% for moderate pain and 50% to 100% for severe pain.
6. Jonathan's feedings were initially decreased to minimize overfeeding, which contributed to his abdominal pain, later changed to "feed to comfort," and then eventually discontinued. At the end of life, children with feeding tubes are highly vulnerable to complications, as intestinal motility slows down and then stops.
7. Jonathan's family was surprised by the length of time from discontinuing his ventilation until he died. They felt blessed by the time they had with him.
8. Jonathan's medical team was surprised by the family's decisions: "I never imagined this family making such decisions." This case is a reminder of the importance of making sure that families have support for all options when new changes are encountered. This approach supports the family-centered care model, with the understanding that the family is in the best position to know what makes the most sense for their child, and that they need to be informed in a way that fully represents all the options available.

Pulmonary edema at the end of life

Grace is a girl who has leukoencephalopathy of unknown etiology with associated hypotonia and intellectual disability. She is nonverbal and nonambulatory and is fed by G tube. She enjoys the many family activities in which she participates.

At 5½ years of age, Grace develops increasing vomiting and associated respiratory symptoms. After a review of contributing factors and intervention options, a plan is developed that includes decreasing G-tube feeding volume by 35%. She is noted to be more comfortable and less puffy, with elimination of vomiting and improvement in respiratory symptoms. Her next 4 weeks are described as the best she has experienced in months.

Grace next develops a respiratory exacerbation that does not improve following initiation of her home management plan. Her parents state, "She sounds like she is drowning in water and is struggling to breathe." She is again noted to develop puffiness. A careful discussion involves the acknowledgment that her body "may be shutting down," resulting in fluid leaking out of the

blood vessels into the tissues of her body. The discussion acknowledges that her feedings may be causing harm and not meeting the parents' goal of comfort for Grace. A care plan includes discontinuing medical fluid and nutrition, other than water used with medications, with ongoing reassessment. Grace is significantly more comfortable the next day, with resolution of her respiratory symptoms and distress. As she continues to do well, a small feeding is tried 3 days later, with a return of respiratory symptoms later in the day. Feedings are again discontinued, and Grace dies 4 days later, peacefully and comfortably in her mother's arms and surrounded by friends and family.

Key points

1. It is imperative to understand the clinical features that can accompany the process of dying. This information can be considered even while reviewing potentially reversible explanations for the clinical findings; the process must be weighed against the harm of further testing or treatment. When informed that the findings might indicate that Grace was dying, her parents felt that any theoretical benefit would be small in comparison with the potential harm of new tests and treatment.
2. Distressing symptoms at the end of life can occur inadvertently (iatrogenic) as a result of ongoing interventions. One example is the risk of excessive fluids and overfeeding in children receiving medical nutrition and fluids through a feeding tube or an IV line.
3. The decision to withhold feedings was based on the overriding goal of maintaining Grace's comfort rather than using an intervention that would contribute to or prolong her suffering.
4. Children who have SNI may be at risk for neurogenic pulmonary edema at the end of life, if changes in the hypothalamus result in further autonomic dysfunction. This is a speculation, based on reports about patients with CNS tumors at the end of life.

TAKE-HOME POINTS

- Multiple problems can contribute to the development of recurrent respiratory illnesses and chronic respiratory symptoms in children who have SNI (table 6.1).
- These problems include impaired mobilization of respiratory secretions / mucus, microaspiration that is often silent, and development of pulmonary inflammation and infection.

- Impairment of the central nervous system results in abnormal motor control, coordination, and tone, all of which can lead to the problems contributing to recurrent respiratory illnesses.
- Recurrent pulmonary illness, often referred to as aspiration pneumonia, is a result of these secondary problems.
- Chronic and acute interventions can provide benefit in maintaining health and can assist with recovery during acute respiratory exacerbations.
- Chronic interventions focus on improving secretion mobilization and minimizing the development of inflammation (table 6.5).
- Anticholinergics for secretion management must balance the goal of decreasing secretion production with the risk of creating thicker secretions that are more difficult to mobilize.
- Antibiotic selection is empirical and should take into account the child's location of care: has the child remained at home, or is the child frequently in the hospital?
- Antibiotic selection for respiratory exacerbations should include anaerobic coverage.
- Antibiotics that can be given by feeding tube include amoxicillin-clavulanate (Augmentin), clindamycin (Cleocin), and fluoroquinolones such as ciprofloxacin and levofloxacin (Levaquin).
- Prophylactic antibiotics—that is, antibiotics given for a prolonged time in an attempt to prevent infection—are not recommended, because of such problems as chronic diarrhea, *Clostridium difficile*, and the development of antibiotic resistance.
- Though the evidence is limited, steroids may provide added benefit, both chronic (inhaled steroids) and acute (5-day prednisone burst).
- The benefit of chronic and acute treatment plans can decrease over time, though often over years, depending on the level of neurological impairment.
- A decline in respiratory health is not a reflection of the care provided in the home or by the medical team; instead, it is a reflection of the contributing problems that cannot be "fixed."
- Surgical interventions, such as Nissen fundoplication, tracheotomy, and spinal surgery, are best considered in the context of other contributing factors that will not be altered by the intervention, and after parents reflect on their child's health trajectory (no decline, a little decline, or a lot of decline from the child's baseline health?).
- Children with the greatest risk of respiratory failure early in life are those that lack a sufficient cough or gag reflex or have an increased

risk of apnea as a result of impairment in the areas of the brain that regulate breathing.

- Dyspnea, also referred to as uncomfortable breathing, should be assessed in children with recurrent respiratory exacerbations that are increasing in frequency.
- Parents can be empowered to recognize dyspnea in their nonverbal child, in the same way that pain features can be identified in nonverbal children.
- Features associated with dyspnea include altered facial expression such as grimacing, appearing restless, having an anxious or fearful look, becoming withdrawn, nasal flaring, grunting, and use of accessory respiratory muscles.
- Management of dyspnea includes a fan directed at the face, repositioning, morphine sulfate, and benzodiazepines for associated anxiety.
- There is an overemphasis on the risk of using morphine sulfate for dyspnea; it is safe when used in a standardized manner, starting with a dose that is 25% to 30% of the dose used for pain, then titrating to benefit; the starting dose can be lowered for those with the greatest compromise.
- When morphine sulfate is discussed as an intervention for distress during respiratory exacerbations, a prescription should be made available for use as needed, rather than waiting until a need arises.
- Morphine sulfate can be used as needed when symptoms are less frequent and scheduled when symptoms occur on most days.
- Home care plans can be beneficial for children who have SNI and recurrent respiratory exacerbations; they allow initiation of acute treatment with an antibiotic and prednisone, based on symptoms, such as when symptoms worsen despite the increased use of chronic treatments, or when fever develops (figure 6.4).
- When recurrent respiratory exacerbations are occurring more frequently, home care plans can incorporate dyspnea treatment along with the use of an antibiotic and steroid.
- Home care plans are more difficult to use for children who do not generate sufficient force from coughing or from respiratory effort to generate "noise"; such children are at increased risk for a "silent" decline in respiratory function and "unexpected" respiratory failure.
- On anticipating a child's increased risk for respiratory failure, it is imperative that discussions about the use of intubation and mechanical support identify the family's hopes, goals, fears, and values that will be part of the decision-making process.

- Other areas to explore when considering resuscitation and the use of mechanical respiratory support include (1) symptom management, to ensure that decisions are not made based on the fear of suffering, and (2) care plan options in the home versus the hospital.

References

Abernethy AP, Currow DC, Frith P, et al. 2003. Randomised, double blind, placebo controlled crossover trial of sustained release morphine for the management of refractory dyspnoea. *BMJ* 327(7414):523–28.

Abernethy AP, McDonald CF, Frith PA, et al. 2010. Effect of palliative oxygen versus room air in relief of breathlessness in patients with refractory dyspnoea: a double-blind, randomised controlled trial. *Lancet* 376(9743):784–93.

Allen S, Raut S, Woollard J, Vassalow M. 2005. Low dose diamorphine reduces breathlessness without causing a fall in oxygen saturation in elderly patients with end-stage idiopathic pulmonary fibrosis. *Palliat Med* 19(2):128–30.

Allewelt M, Schuler P, Bolcskei PL, et al. 2004. Ampicillin + sulbactam vs clindamycin +/– cephalosporin for the treatment of aspiration pneumonia and primary lung abscess. *Clin Microbiol Infect* 10:163–70.

Amsden GW. 2005. Anti-inflammatory effects of macrolides: an underappreciated benefit in the treatment of community-acquired respiratory tract infections and chronic inflammatory pulmonary conditions? *J Antimicrob Chemother* 55(1):10–21.

Arvedson JC. 2008. Assessment of pediatric dysphagia and feeding disorders: clinical and instrumental approaches. *Dev Disabil Res Rev* 14(2):118–27.

Baikie G, South MJ, Reddihough DS, et al. 2005. Agreement of aspiration tests using barium videofluoroscopy, salivagram, and milk scan in children with cerebral palsy. *Dev Med Child Neurol* 47(2):86–93.

Bellon A, Perez-Garcia G, Coverdale JH, Chacko RC. 2009. Seizures associated with levofloxacin: case presentation and literature review. *Eur J Clin Pharmacol* 65(10):959–62.

Berry JG, Graham DA, Graham RJ, et al. 2009. Predictors of clinical outcomes and hospital resource use of children after tracheotomy. *Pediatrics* 124(2):563–72.

Boesch RP, Daines C, Willging JP, et al. 2006. Advances in the diagnosis and management of chronic pulmonary aspiration in children. *Eur Respir J* 28(4):847–61.

Bramow S, Faber-Rod JC, Jacobsen C, et al. 2008. Fatal neurogenic pulmonary edema in a patient with progressive multiple sclerosis. *Mult Scler* 14(5):711–15.

Brook I. 1996. Treatment of aspiration or tracheostomy-associated pneumonia in neurologically impaired children: effect of antimicrobials effective against anaerobic bacteria. *Int J Pediatr Otorhinolaryngol* 35:171–77.

Brook I. 2004. Role of anaerobic bacteria in infections following tracheostomy, intubation, or the use of ventilatory tubes in children. *Ann Otol Rhinol Laryngol* 113(10):830–34.

Brook I, Finegold SM. 1980. Bacteriology of aspiration pneumonia in children. *Pediatrics* 65:1115–20.

Brown LK. 2010. Hypoventilation syndromes. *Clin Chest Med* 31(2):249–70.

Brown SJ, Eichner SF, Jones JR. 2005. Nebulized morphine for relief of dyspnea due to chronic lung disease. *Ann Pharmacother* 39(6):1088–92.

Browne TR. 1978. Clonazepam. *N Engl J Med* 299(15):812–16.

Campbell ML. 2008. Psychometric testing of a respiratory distress observation scale. *J Palliat Med* 11(1):44–50.

Campbell ML. 2010. Assessing respiratory distress when the patient cannot report dyspnea. *Nurs Clin North Am* 45(3):363–73.

Campbell ML, Templin T, Walch J. 2010. A respiratory distress observation scale for patients unable to self-report dyspnea. *J Palliat Med* 13(3):285–90.

Carron JD, Derkay CS, Strope GL, et al. 2000. Pediatric tracheotomies: changing indications and outcomes. *Laryngoscope* 110(7):1099–104.

Cheung KM, Tse HW, Tse PW, Chan KH. 2006. Nissen fundoplication and gastrostomy in severely neurologically impaired children with gastroesophageal reflux. *Hong Kong Med J* 12(4):282–88.

Chowdhury BA, Dal Pan G. 2010. The FDA and safe use of long-acting beta-agonists in the treatment of asthma. *N Engl J Med* 362(13):1169–71.

Clemens KE, Klaschik E. 2007. Symptomatic therapy of dyspnea with strong opioids and its effect on ventilation in palliative care patients. *J Pain Symptom Manage* 33(4):473–81.

Clemens KE, Klaschik E. 2011. Dyspnoea associated with anxiety-symptomatic therapy with opioids in combination with lorazepam and its effect on ventilation in palliative care patients. *Support Care Cancer* 19(12):2027–33.

Cline JM, Woods CR, Ervin SE, et al. 2012. Surveillance tracheal aspirate cultures do not reliably predict bacteria cultured at the time of an acute respiratory infection in children with tracheostomy tubes. *Chest* 141(3):625–31.

Cook SP, Lawless ST, Kettrick R. 1996. Patient selection for primary laryngotracheal separation as treatment of chronic aspiration in the impaired child. *Int J Pediatr Otorhinolaryngol* 38(2):103–13.

Di Lorenzo C, Orenstein S. 2002. Fundoplication: friend or foe? *J Pediatr Gastroenterol Nutr* 34(2):117–24.

Dreyfuss D. 2001. Aspiration pneumonia (letter). *N Engl J Med* 344:1868.

Drobnic ME, Suñé P, Montoro JB, et al. 2005. Inhaled tobramycin in non-cystic fibrosis patients with bronchiectasis and chronic bronchial infection with *Pseudomonas aeruginosa*. *Ann Pharmacother* 39(1):39–44.

Eastham KM, Fall AJ, Mitchell L, Spencer DA. 2004. The need to redefine non-cystic fibrosis bronchiectasis in childhood. *Thorax* 59(4):324–27.

Elman LB, Dubin RM, Kelley M, McCluskey L. 2005. Management of oropharyngeal and tracheobronchial secretions in patients with neurologic disease. *J Palliat Med* 8(6):1150–59.

Fahy JV, Dickey BF. 2010. Airway mucus function and dysfunction. *N Engl J Med* 363(23): 2233–47.

Fawcett HD, Hayden CK, Adams JC, Swischuk LE. 1988. How useful is gastroesophageal reflux scintigraphy in suspected childhood aspiration? *Pediatr Radiol* 18(4):311–13.

Feudtner C, Carroll KW, Hexem KR, et al. 2010. Parental hopeful patterns of thinking, emotions, and pediatric palliative care decision making: a prospective cohort study. *Arch Pediatr Adolesc Med* 164(9):831–39.

Galbraith S, Fagan P, Perkins P, et al. 2010. Does the use of a handheld fan improve chronic dyspnea? A randomized, controlled, crossover trial. *J Pain Symptom Manage* 39(5): 831–38.

Genecov DG, Barceló CR, Steinberg D, et al. 2009. Clinical experience with the application of distraction osteogenesis for airway obstruction. *J Craniofac Surg* 20(Suppl 2):1817–21.

Gleeson K, Eggli DF, Maxwell SL. 1997. Quantitative aspiration during sleep in normal subjects. *Chest* 111(5):1266–72.

Goeminne P, Dupont L. 2010. Non-cystic fibrosis bronchiectasis: diagnosis and management in 21st century. *Postgrad Med J* 86(1018):493–501.

Goldin AB, Sawin R, Seidel KD, Flum DR. 2006. Do antireflux operations decrease the rate of reflux-related hospitalizations in children? *Pediatrics* 118(6):2326–33.

Hatakeyama S, Tachibana A, Suzuki H, Okano H. 1995. Treatment of aspiration pneumonia with low-dose methylprednisolone and antibiotics. *Nihon Kyobu Shikkan Gakkai Zasshi* 33(1):51–56.

Hauer J, Mackey D. 2012. Treatment with gabapentin associated with resolution of apnea in two infants with neurologic impairment. *J Palliat Med* [Epub ahead of print].

Hauer JM. 2007. Respiratory symptom management in a child with severe neurologic impairment. *J Palliat Med* 10(5):1201–7.

Homnick DN. 2007. Mechanical insufflation-exsufflation for airway mucus clearance. *Respir Care* 52(10):1296–305; discussion 1306–7.

Huxley EJ, Viroslav J, Gray WR, Pierce AK. 1978. Pharyngeal aspiration in normal adults and patients with depressed consciousness. *Am J Med* 64(4):564–68.

Ize-Ludlow D, Gray JA, Sperling MA, et al. 2007. Rapid-onset obesity with hypothalamic dysfunction, hypoventilation, and autonomic dysregulation presenting in childhood. *Pediatrics* 120(1):e179–88.

Javaheri S. 2010. Central sleep apnea. *Clin Chest Med* 31(2):235–48.

Kadowaki M, Demura Y, Mizuno S, et al. 2005. Reappraisal of clindamycin IV monotherapy for treatment of mild-to-moderate aspiration pneumonia in elderly patients. *Chest* 127:1276–82.

Katz ES, D'Ambrosio CM. 2010. Pediatric obstructive sleep apnea syndrome. *Clin Chest Med* 31(2):221–34.

Katz ES, McGrath S, Marcus CL. 2000. Late-onset central hypoventilation with hypothalamic dysfunction: a distinct clinical syndrome. *Pediatr Pulmonol* 29(1):62–68.

Kawahara H, Okuyama H, Kubota A, et al. 2004. Can laparoscopic antireflux surgery improve the quality of life in children with neurologic and neuromuscular handicaps? *J Pediatr Surg* 39(12):1761–64.

Le J, Ashley ED, Neuhauser MM, et al., Society of Infectious Diseases Pharmacists Aerosolized Antimicrobials Task Force. 2010. Consensus summary of aerosolized antimicrobial agents: application of guideline criteria. Insights from the Society of Infectious Diseases Pharmacists. *Pharmacotherapy* 30(6):562–84.

Lee JS, Collard HR, Raghu G, et al. 2010. Does chronic microaspiration cause idiopathic pulmonary fibrosis? *Am J Med* 123(4):304–11.

Lee SL, Shabatian H, Hsu JW, et al. 2008. Hospital admissions for respiratory symptoms and failure to thrive before and after Nissen fundoplication. *J Pediatr Surg* 43(1):59–63; discussion 63–65.

Mack JW, Wolfe J, Cook EF, et al. 2007. Hope and prognostic disclosure. *J Clin Oncol* 25(35):5636–42.

Mack JW, Wolfe J, Grier HE, et al. 2006. Communication about prognosis between parents and physicians of children with cancer: parent preferences and the impact of prognostic information. *J Clin Oncol* 24(33):5265–70.

Macleod AD. 2002. Neurogenic pulmonary edema in palliative care. *J Pain Symptom Manage* 23(2):154–56.

Mandell DL, Yellon RF, Bradley JP, et al. 2004. Mandibular distraction for micrognathia and severe upper airway obstruction. *Arch Otolaryngol Head Neck Surg* 130(3):344–48.

Marcus CL. 2001. Sleep-disordered breathing in children. *Am J Respir Crit Care Med* 164(1): 16–30.

Marik PE. 2001. Aspiration pneumonitis and aspiration pneumonia. *N Engl J Med* 344(9): 665–71.

Mazzocato C, Buclin T, Rapin CH. 1999. The effects of morphine on dyspnea and ventilatory function in elderly patients with advanced cancer: a randomized double-blind controlled trial. *Ann Oncol* 10(12):1511–14.

McCarty SF, Gaebler-Spira D, Harvey RL. 2001. Improvement of sleep apnea in a patient with cerebral palsy. *Am J Phys Med Rehabil* 80(7):540–42.

Miske LJ, Hickey EM, Kolb SM, et al. 2004. Use of the mechanical in-exsufflator in pediatric patients with neuromuscular disease and impaired cough. *Chest* 125(4):1406–12.

Morton RE, Wheatley R, Minford J. 1999. Respiratory tract infections due to direct and reflux aspiration in children with severe neurodisability. *Dev Med Child Neurol* 41(5):329–34.

Mousa H, Caniano DA, Alhajj M, et al. 2006. Effect of Nissen fundoplication on gastric motor and sensory functions. *J Pediatr Gastroenterol Nutr* 43(2):185–89.

Nagase T, Fukuchi Y, Teramoto S, et al. 1991. Intravenous bolus of prednisolone decreases 15-hydroxyeicosaetraenoic acid formation in the rat model of acid aspiration. *Crit Care Med* 19(7):950–54.

Navigante AH, Cerchietti LC, Castro MA, et al. 2006. Midazolam as adjunct therapy to morphine in the alleviation of severe dyspnea perception in patients with advanced cancer. *J Pain Symptom Manage* 31(1):38–47.

Plioplys AV, Lewis S, Kasnicka I. 2002. Pulmonary vest therapy in pediatric long-term care. *J Am Med Dir Assoc* 3(5):318–21.

Rapoport A. 2010. Sublingual atropine drops for the treatment of pediatric sialorrhea. *J Pain Symptom Manage* 40(5):783–88.

Raval TH, Elliott CA. 2008. Botulinum toxin injection to the salivary glands for the treatment of sialorrhea with chronic aspiration. *Ann Otol Rhinol Laryngol* 117(2):118–22.

Richards CA, Milla PJ, Andrews PL, Spitz L. 2001. Retching and vomiting in neurologically impaired children after fundoplication: predictive preoperative factors. *J Pediatr Surg* 36(9):1401–4.

Rogers DF. 2007. Mucoactive agents for airway mucus hypersecretory diseases. *Respir Care* 52(9):1176–93; discussion 1193–97.

Rubin BK. 2007. Mucolytics, expectorants, and mucokinetic medications. *Respir Care* 52(7): 859–65.

Rubin BK. 2008. Aerosolized antibiotics for non-cystic fibrosis bronchiectasis. *J Aerosol Med Pulm Drug Deliv* 21(1):71–76.

Rusakow LS, Guarín M, Wegner CB, et al. 1998. Suspected respiratory tract infection in the tracheostomized child: the pediatric pulmonologist's approach. *Chest* 113(6):1549–54.

Schechter MS. 2007. Airway clearance applications in infants and children. *Respir Care* 52(10):1382–90; discussion 1390–91.

Shinkai M, Rubin BK. 2005. Macrolides and airway inflammation in children. *Paediatr Respir Rev* 6(3):227–35.

Simon ST, Higginson IJ, Booth S, et al. 2010. Benzodiazepines for the relief of breathlessness in advanced malignant and non-malignant diseases in adults. *Cochrane Database Syst Rev* (1):CD007354.

Sjögren P, Nilsson E, Forsell M, et al. 2008. A systematic review of the preventive effect of oral hygiene on pneumonia and respiratory tract infection in elderly people in hospitals and nursing homes: effect estimates and methodological quality of randomized controlled trials. *J Am Geriatr Soc* 56(11):2124–30.

Smith CD, Othersen HB Jr, Gogan NJ, Walker JD. 1992. Nissen fundoplication in children with profound neurologic disability: high risks and unmet goals. *Ann Surg* 215(6): 654–58.

Sritippayawan S, Kun SS, Keens TG, Davidson Ward SL. 2003. Initiation of home mechanical ventilation in children with neuromuscular diseases. *J Pediatr* 142(5):481–85.

Srivastava R, Berry JG, Hall M, et al. 2009. Reflux related hospital admissions after fundoplication in children with neurological impairment: retrospective cohort study. *BMJ* 339:b4411.

Srivastava R, Downey EC, O'Gorman M, et al. 2009. Impact of fundoplication versus gastrojejunal feeding tubes on mortality and in preventing aspiration pneumonia in young children with neurologic impairment who have gastroesophageal reflux disease. *Pediatrics* 123(1):338–45.

Stafler P, Carr SB. 2010. Non-cystic fibrosis bronchiectasis: its diagnosis and management. *Arch Dis Child Educ Pract Ed* 95(3):73–82.

Stein MR. 2003. Possible mechanisms of influence of esophageal acid on airway hyperresponsiveness. *Am J Med* 115(Suppl 3A):55–59S.

Temel JS, Greer JA, Muzikansky A, et al. 2010. Early palliative care for patients with metastatic non-small-cell lung cancer. *N Engl J Med* 363(8):733–42.

Tsirikos AI, Chang WN, Dabney KW, et al. 2003. Life expectancy in pediatric patients with cerebral palsy and neuromuscular scoliosis who underwent spinal fusion. *Dev Med Child Neurol* 45(10):677–82.

van Gestel JP, Robroch AH, Bollen CW, et al. 2010. Mechanical ventilation for respiratory failure in children with severe neurological impairment: is it futile medical treatment? *Dev Med Child Neurol* 52(5):483–88.

Vijayasekaran S, Unal R, Schraff SA, et al. 2007. Salivary gland surgery for chronic pulmonary aspiration in children. *Int J Pediatr Otorhinolaryngol* 71(1):119–23.

Wales PW, Diamond IR, Dutta S, et al. 2002. Fundoplication and gastrostomy versus image-guided gastrojejunal tube for enteral feeding in neurologically impaired children with gastroesophageal reflux. *J Pediatr Surg* 37(3):407–12.

Wolfe J, Klar N, Grier HE, et al. 2000. Understanding of prognosis among parents of children who died of cancer: impact on treatment goals and integration of palliative care. *JAMA* 284(19):2469–75.

Yuan N, Kane P, Shelton K, et al. 2010. Safety, tolerability, and efficacy of high-frequency chest wall oscillation in pediatric patients with cerebral palsy and neuromuscular diseases: an exploratory randomized controlled trial. *J Child Neurol* 25(7):815–21.

Zocratto OB, Savassi-Rocha PR, Paixao RM, Salles JM. 2006. Laryngotracheal separation surgery: outcome in 60 patients. *Otolaryngol Head Neck Surg* 135(4):571–75.

CHAPTER 7

Problems of the Central Nervous System

Spasticity, Dystonia, Dysautonomia, Seizures, and Related Problems

The fibers of all things have their tension and are strained like the strings of an instrument.
—Henry David Thoreau

Nearly all children and young adults who have severe neurological impairment have one or more of the problems covered in this chapter. Impairment of the central nervous system can result in abnormal muscle tone, uncontrolled movement, dysfunction of the autonomic nervous system, seizures, agitation, and changes in level of alertness.

OVERVIEW OF PROBLEMS OF THE CENTRAL NERVOUS SYSTEM

When the central nervous system is impaired, there can be an imbalance between the signals sent from and received by the brain. The signals (information) are transmitted by neurotransmitters (chemicals) that stimulate the receptors of nerve cells, or neurons. These chemical signals activate or inhibit nerve cell receptors, allowing nerve cells to communicate with each other.

Damage in the CNS can alter the suppression and stimulation of signals sent to and from the brain. A multitude of problems may result, both chronically and intermittently, including spasticity, muscle spasms, dystonia, autonomic dysfunction, and tonic posturing.

Many of the medications used to treat these problems provide benefit by either enhancing inhibition or decreasing excitation of signals. Many of the treatments do not "fix" the source of the problem but rather alter the imbalance. Some medications enhance inhibition by potentiating GABA

(gamma-aminobutyric acid), an inhibitory neurotransmitter. Others decrease excitation by inhibiting glutamate, an excitatory neurotransmitter. In other cases, the type of receptor determines whether the neurotransmitter produces excitation or inhibition of the signal. Blocking the receptor then has the opposite effect. A simple description of this approach to treatment is to say that medications are used to "calm" the imbalance in the nervous system.

Some children benefit from the use of several medications with different mechanisms of action. This potential benefit must always be weighed against the potential risk associated with each medication. The section "Identifying a medication treatment plan" in chapter 3 can help with decision making at each step of a medication trial.

General management of CNS problems

Each of the problems reviewed in this chapter can worsen as a result of any factor that alters a child's comfort, such as pain, illness, constipation, disrupted sleep, and medication toxicity. Paying attention to all of these contributing issues can improve overall care. Each of the reviewed problems benefits from general care plans that minimize distress and discomfort.

Interventions that can decrease the severity of CNS problems include a regular sleep cycle, a calm and familiar environment, and an effective bowel regimen. In addition, integrative therapies, or nonpharmacological interventions, are as important in care plans as are the medication options. These interventions include comfort strategies reviewed in chapter 4, such as cuddling, rocking, massaging, repositioning, and music. Other beneficial approaches include physical therapy, supportive cushions, vibrating mats and pillows, weighted blankets, a cool fan, and water baths (including baths with soft jets). Other modalities for consideration, though less studied, include aromatherapy and acupuncture.

General concerns about CNS problems

Each of the problems reviewed in this chapter has the potential to become persistent and intractable. As problems escalate or persist, the initial focus is on managing any triggers of the problem along with medication trials directed at the problem itself. Most children will experience improvement with careful attention to contributing factors and treatment options, but the degree and duration of benefit will vary.

This process needs to be balanced with considerations of the risk associated with multiple medication trials, especially when multiple medications are in use. This is a time to "take a step back" to assess all aspects of the child's health, such as noting when problems in more than one area may be indicating an irreversible decline of the CNS and when problems that are persisting are affecting the comfort of the child. In this chapter I review the management of each problem that can increase the likelihood of improving outcomes. Chapter 9 provides greater detail about approaches to care plans when problems remain intractable.

HYPERTONIA, SPASTICITY, AND MUSCLE SPASMS

Muscle tone is controlled by inhibitory (relaxing) signals from the CNS to the muscles and excitatory (stimulating) signals from the muscles to the CNS. Increased tone is common in children who have SNI as a result of upper motor neuron injury—damage to nerve cells in the motor region of the cerebral cortex or in the brain stem. This injury to the CNS results in loss of voluntary control of muscles and the normal inhibitory control over muscle tone. Other indications of upper motor neuron injury include muscle weakness, exaggerated deep tendon reflexes, and clonus, which is involuntary muscle contractions due to sudden stretching of the muscle, most commonly at the ankle.

Hypertonia is the increased resistance of muscle to externally imposed movement (referred to as passive movement) that is not dependent on the velocity (speed) of the movement. It can occur with or without spasticity. Spasticity is a specific type of hypertonia, defined as an involuntary, velocity-dependent increase in muscle tone that results in resistance of the muscles to movement (Sanger et al. 2003). Finally, a muscle spasm is a sudden, involuntary contraction of a muscle or group of muscles.

Spasticity is assessed by measuring the resistance of the muscle to passive lengthening with varying degrees of velocity, when the muscle is in its most relaxed state. When the muscle is stretched and lengthened, resistance to movement increases. One scale used to assess the level of resistance to passive movement about a joint with varying degrees of velocity is the modified Ashworth scale (table 7.1).

The goal of treatment is to lessen the unwanted effects of increased tone. Treatment is intended to improve comfort, minimize the development of contractures and musculoskeletal deformities, improve ease of care of the child, and perhaps improve function. Treatment to decrease tone must be balanced with potential unwanted effects, such as a further

TABLE 7.1 Modified Ashworth scale

Grade	Description
0	No increase in muscle tone
1	Slight increase in muscle tone, manifested by a catch and release or by minimal resistance at the end of the range of motion (ROM) when the affected part(s) moved in flexion or extension
1+	Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the ROM
2	More marked increase in muscle tone through most of the ROM, but affected part(s) easily moved
3	Considerable increase in muscle tone, passive movement difficult
4	Affected part(s) rigid in flexion and extension

decrease in trunk and neck tone, which would make it more difficult for the child to maintain his or her head in an upright position.

One concern is the development of pain, though spasticity itself is typically not painful. Pain can occur when increased tone results in musculoskeletal inflammation and injury. Interventions that decrease tone can also decrease inflammation and injury and thus pain. Medications such as nonsteroidal anti-inflammatory drugs can offer relief if pain is caused by musculoskeletal inflammation or injury. Muscle spasms can also result in pain. Other sources of pain must be considered as the possible trigger for an increase in spasticity and intermittent muscle spasms. Other factors that can increase tone and spasticity include illness and anxiety.

Treatment

Therapeutic interventions to treat spasticity include physical therapy, oral medications, injectable medications, and a surgically placed intrathecal baclofen pump. Consideration of medical interventions can include a multidisciplinary team of physical therapists, physiatrists, neurologists, orthopedic surgeons, and pain specialists.

Botulinum toxin

For localized or segmental spasticity, current evidence indicates that botulinum toxin type A (Botox) is effective at reducing spasticity and associated pain in children who have cerebral palsy (Delgado et al. 2010; Lundy,

Lumsden, and Fairhurst. 2009; Rivard, Nugent, and Symons 2009). The duration of effect can vary from 3 to 6 months. Factors that may decrease this duration include severe spasticity, an inadequate dose, the presence of a fixed contracture, or a growth spurt.

Medications

Medications for generalized spasticity include diazepam, baclofen, alpha-2 receptor agonists (clonidine and tizanidine), dantrolene, and gabapentin (Krach 2001). Practice guidelines from the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society recommend diazepam for the short-term treatment of spasticity in children who have cerebral palsy (Delgado et al. 2010). Tizanidine may also be considered, though there is less evidence about its benefit (Delgado et al. 2010). The other studies, as reviewed by the American Academy of Neurology and the Child Neurology Society, were inadequate to confirm evidence of benefit from baclofen, dantrolene, and clonidine, though these medications can be beneficial for some children (Delgado et al. 2010; Krach 2001; Lubsch et al. 2006; Montané, Vallano, and Laporte 2004). Though not studied in children, gabapentin has proved beneficial for spasticity in adults with multiple sclerosis (MS). In a double-blind placebo-controlled trial, adults with MS who were treated with gabapentin had a significant reduction in spasticity without secondary sedation (Cutter et al. 2000). Side effects common to the oral medications include sedation, drowsiness, and muscle weakness that is dose related (Krach 2001). The uses and properties of these medications are summarized below.

BENZODIAZEPINES

- Diazepam may be best used intermittently for painful muscle spasms that persist rather than chronically for spasticity, because tolerance develops with chronic use.
- Other benzodiazepines have muscle relaxant properties, making them potential options for intermittent muscle spasms.

CLONIDINE AND TIZANIDINE: ALPHA-2 RECEPTOR AGONISTS

- Clonidine's side effects include hypotension (low blood pressure), bradycardia (low heart rate), and sedation; treatment should start with one dose a day to minimize the likelihood of these effects, with an increase in dose every 3 to 4 days, as tolerated.

- The side effect of hypotension is less significant for children unable to stand—this eliminates the risk of standing and falling, with resulting injury, as the result of orthostatic hypotension (when the blood pressure drops further on standing).
- One study looked at the clonidine doses used for treating children who had spasticity; the authors identified an average dose of 0.4 mg/day, with an average dose based on weight of 0.02 mg/kg/day, and a recommended maximum dose of 1.8 mg/day (Lubsch et al. 2006).
- Tizanidine's side effects include sedation, agitation, irritability, and insomnia; significantly fewer adverse events occur in children than in adults, including fewer episodes of low blood pressure or low heart rate. The risk of elevated liver transaminases (ALT and AST) in children was identified mostly when tizanidine was taken in combination with other medications that can result in hepatotoxicity (liver damage) (Henney and Chez 2009).
- Ciprofloxacin should not be used for patients taking tizanidine, because ciprofloxacin increases the tizanidine level by decreasing its metabolism (Henney and Chez 2009).
- Clonidine and tizanidine may also decrease pain with mild antinociceptive properties, through substance P modulation (Semenchuk and Sherman 2000; H. Smith and Elliott 2001).
- Clonidine and tizanidine should be tapered off over 2 to 3 weeks to avoid rebound hypertension.

GABAPENTIN

- Gabapentin's side effects include sedation, nystagmus (jerky eye movements), tremor, ataxia, and swelling.
- Gabapentin for spasticity has mostly been studied in patients with multiple sclerosis.

BACLOFEN

- A sudden cessation of baclofen results in withdrawal symptoms that include agitation, confusion, hallucinations, insomnia, hyperthermia, seizures, rebound spasticity, and muscle rigidity (Leo and Baer 2005).
- Because baclofen cannot be given intravenously and is not absorbed rectally, it is important to plan a taper schedule over 2 to 3 weeks prior to any procedure that may result in ileus (nonmechanical bowel obstruction), such as decreasing by 10% to 20% every 2 to 3 days, or a slower taper if symptoms occur.

- One study suggested the following baclofen dosages for children: younger than 2 years, 10 to 20 mg/day (maximum 40 mg/day); 2 to 7 years, 20 to 30 mg/day (maximum 60 mg/day); and older than 8 years, 30 to 40 mg/day (maximum 200 mg/day)—in divided doses titrated to the patient's response and/or adverse effects (Lubsch et al. 2006).

DANTROLENE

- Dantrolene has its effect on skeletal muscle rather than on the brain, by inhibiting the release of calcium in muscle cells (from the sarcoplasmic reticulum) and thus abolishing electrical stimulation of muscle contraction; for this reason, weakness is a common side effect.
- Dantrolene has been associated with hepatotoxicity in adults and with elevated liver enzymes (ALT and AST) in children; liver enzyme levels should be measured before starting and periodically while taking this drug. It is prudent to minimize the use of other potentially hepatotoxic medications, such as valproic acid.
- Dantrolene should be used cautiously, because it has the highest frequency of side effects with limited evidence of benefit.

Intrathecal baclofen pump

Intrathecal baclofen (ITB), delivered through a pump as a continuous infusion into the intrathecal space of the spinal cord, has been demonstrated to decrease spasticity of cerebral origin (Albright et al. 1993; Hoving et al. 2009). The pump is placed just below the skin of the abdomen, with a tube connected to the base of the spine. The baclofen bathes the nerves in the area of the tube, delivering a continuous dose that is one-thousandth the required oral dose, minimizing such side effects as sleepiness. Serious complications of an ITB pump include infection and sudden malfunction of the pump.

Before the pump is implanted, a trial of baclofen is performed, either by lumbar puncture or after placement of a catheter. ITB is intended to treat spasticity of the lower extremities. Intrathecally delivered baclofen can also reduce dystonia, so ITB can benefit some children with mixed spasticity and dystonia (Albright et al. 1996; Albright et al. 2001). Intrathecal baclofen was also shown to reduce pain in 17 children who had intractable cerebral palsy (Hoving et al. 2009). One case report found a beneficial effect for a boy who had adrenoleukodystrophy, a neurodegenerative condition

(Chu, Sala, and Weiner 2001). The baclofen dose delivered can be adjusted, allowing optimized treatment.

The ITB pump needs to be refilled every 3 months and must be replaced when the battery loses power, typically after 4 or 5 years. The benefit of intrathecally delivered baclofen is a lower incidence of cerebral side effects, such as sedation, with a greater reduction in tone. This must be weighed against the complication risk of ITB. Complications affect up to 20% of patients and include meningitis (infection of the membranes lining the spinal cord and brain), infection of the tissue surrounding the pump (cellulitis), and malfunction of the tube (Albright et al. 1996). In another study, the most common complications of the surgery were tube-related problems (31%), seromas and fluid pockets (24%), and cerebrospinal fluid leaks (15%) (Albright et al. 2003). These complications may require hospitalization for IV antibiotics or surgical intervention. A sudden stop of baclofen delivery as a result of tube displacement or kinking can cause the same symptoms as an abrupt stop of oral baclofen (Zuckerbraun et al. 2004).

Selective dorsal rhizotomy (SDR) is another surgical intervention for spasticity, though it is not a useful option for children who have SNI. In general, SDR is ideally suited for children 4 to 8 years old with spastic diplegia (typically, children born prematurely) who are ambulatory and cognitively intact (Sgouros 2007).

Summary of features of spasticity and the treatment options

- Pain and other problems that can trigger and exacerbate spasticity and muscle spasms must be considered. Information about pain treatment is covered in detail in chapter 4.
- Defining the goals of treatment at the outset will help determine when to continue or stop a treatment trial, and when to consider another intervention. Defining goals may include assessing any of the following:
  - What is the child's tone prior to treatment?
  - Does the child have spasticity on examination—that is, velocity-dependent resistance to passive movement? If so, what is the child's level of spasticity?
  - How often does the child experience muscle spasms in a typical day?
  - Does the child have episodes of arching, posturing, "toning," or stiffening?

  - — Does the child appear to be in pain before or during muscle spasms? Do comfort measures such as repositioning, cuddling, or massage help lessen spasms?
- This baseline information can then be used to "measure" and follow the degree of benefit from any treatment. Follow-up assessment can include the following:
  - — What degree of benefit do you see in your child since treatment started? Is it easier to provide such care as clothing, bathing, and transferring? Do you consider your child to be a little or a lot better—25%, 50%, or more than 50% better?
  - — Has there been a decrease in the frequency and severity of muscle spasms and associated features such as arching or stiffening?
  - — Is your child more comfortable?
  - — How does the clinical examination since treatment started compare with the initial exam?
- Gabapentin and alpha-2 receptor agonists such as clonidine may have a preferential role in treating spasticity in children who have SNI and pain behaviors, given the challenge of distinguishing whether pain is secondary to muscle spasms or is triggering the spasms. Of the alpha-2 receptor agonists, clonidine has an advantage in delivery options, including liquid and transdermal patch.
- A medication trial directed at pain should be considered for persistent and troublesome spasticity and should be carried out before placement of an intrathecal baclofen pump.
- Diazepam or other benzodiazepines can be beneficial when used in the short term or as needed for intermittent muscle spasms.
- Other medications for the treatment of spasticity include baclofen and dantrolene.
- Injection of botulinum toxin type A is beneficial for spasticity that is localized to a group of muscles.
- Intrathecal baclofen pump is beneficial for generalized spasticity that persists despite medication trials for spasticity and for pain.

Lucas is an 8-year-old who suffered an anoxic brain injury as a result of a near-drowning event. He has a history of significant spasticity, treated with baclofen, and is currently taking 15 mg four times per day. During a routine examination, he is noted to have low tone in all his extremities, including with passive movement at increasing velocity. In a review of his history, several sources of pain were identified and treated following an increase in his

baclofen dose to its current level. His baclofen is now decreased until his tone is slightly increased. At this lower baclofen level, Lucas is more alert and remains comfortable, without concerns about significant spasticity.

Aaron is an 18-year-old with cerebral palsy. He has a history of significant spasticity, treated with baclofen, 20 mg four times daily, and diazepam, 2 mg three times daily, and is taking carbamazepine for epilepsy. His tone has been increasing over the past year, making it difficult to provide daily care and resulting in frequent skin rashes under his arms. He is described as "very tight, making it hard to dress him, bathe him, and keep the skin under his arms dry." He has no intermittent muscle spasms or discomfort. A clonidine trial is initiated, with a significant decrease in tone noted in the first week with a dose of 0.1 mg twice daily, further improvement as the dose is increased to 0.1 mg three times daily, and no sedation. He is described as "much more relaxed, smiling more, with a significant improvement in the ability to provide care." The option remains to further increase the dose, as needed.

DYSTONIA

Dystonia is a movement disorder in which involuntary sustained or intermittent muscle contractions cause twisting and repetitive movements, abnormal postures, or both (Bressman 2000; Sanger et al. 2010). Dystonia can be a primary disorder of movement, or secondary to diseases of and insults to the CNS, or caused by medications such as neuroleptics and other drugs that are dopamine-2 (D-2) receptor blockers. Children who have SNI typically have secondary dystonia. Dystonia can be triggered or exacerbated by illness, pain, emotional distress, and certain medications. Severe dystonia, typically escalating from baseline as a result of one of these triggers, can occasionally result in rhabdomyolysis (muscle fiber breakdown), with a risk of acute renal (kidney) failure (Mariotti et al. 2007; Watemberg et al. 2000).

Treatment

Interventions for dystonia include physical therapy, botulinum toxin for focal muscle groups, medications, and surgery. Medications that cause dystonic reactions include metoclopramide, haloperidol, and risperidone, all D-2 receptor blockers. Along with stopping any such medication, diphenhydramine or benztropine can be used to treat medication-induced dystonic reactions.

A few studies have evaluated the effectiveness of medications for secondary dystonia; they assessed benzodiazepines, anticholinergics such as trihexyphenidyl and benztropine, baclofen, dopaminergic agents such as bromocriptine and levodopa, and tetrabenazine, a dopamine depletor and blocker (Jankovic 2009).

Surgical interventions may be considered for children with intractable dystonia who have not responded to medical therapy. Intrathecally delivered baclofen has been shown to reduce generalized dystonia, including in people who have global severe neurological impairment (Albright et al. 1996; Albright et al. 2001). Another surgical option is deep brain stimulation (DBS) of the globus pallidus, studied mostly in people who have primary forms of dystonia, with less benefit noted for people who have secondary dystonia (Kupsch et al. 2003; Lundy, Doherty, and Fairhurst 2009).

As with the other problems reviewed in this chapter, it is important to consider pain as an underlying trigger of dystonia. Some children who have SNI may benefit from an empirical medication trial directed at sources such as central pain. Such medication trials should be conducted before pursuing surgical interventions.

CHOREA

Chorea is characterized by abrupt, irregular, chaotic, involuntary movements that can range from tiny fidgeting to more obvious dancelike movements that tend to flow from body part to body part (Sanger et al. 2010). Emotional stress, fatigue, and pain can make the movements worse. Primary chorea is often attributable to acute rheumatic fever. Secondary chorea can be seen in a number of neurodegenerative conditions. Many drugs, notably metoclopramide (Reglan), haloperidol (Haldol), phenothiazines such as proclorperazine (Compazine) and promethazine (Phenergan), and phenytoin (Dilantin), can also induce choreiform movement.

Treatment

Chorea is often not painful but can be distressing to watch. The goals of treatment include improved positioning, increased purposeful movement if possible, and decreased risk of injury. Routine care plans that may decrease movement include a low-stimulation environment, sleep cycle regulation, an effective bowel regimen, repositioning, padding or physical barriers to prevent injury, physical therapy, a familiar environment,

and a cool fan. Medications, when used, include those indicated for pain (when present), valproic acid, carbamazepine, and tetrabenazine (Jankovic 2009).

MYOCLONUS

Myoclonic movements are brief, abrupt, shocklike, nonsuppressible, involuntary movements that are due to sudden contraction or relaxation of one or more muscles (Caviness 2009; Mink and Zinner 2010). Myoclonus looks like a quick startle.

Myoclonus can be classified as part of a chronic seizure disorder or as secondary to diseases or injuries of the CNS. Secondary myoclonus is also referred to as cortical myoclonus. Secondary myoclonus can be a result of many inborn errors of metabolism as well as severe injury to the CNS, such as hypoxic-ischemic encephalopathy (Caviness 2009; Mink and Zinner 2010). Myoclonus can also occur with renal failure, liver failure, hypoglycemia (low blood glucose), and hyponatremia (low serum sodium).

In case reports, medications implicated in causing myoclonus include fluoroquinolone antibiotics such as levofloxacin, anticonvulsants (phenytoin, lamotrigine, phenobarbital, gabapentin, pregabalin), tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), cannabinoids, tramadol, and high doses of opioids. Combining such medications may further increase the risk. Myoclonus that results from a medication is usually generalized and may be provoked by a stimulus.

Treatment

Treatment is considered when myoclonus is frequent and is a source of distress to the child. Consideration should be given to discontinuing medications, though the benefit of the medication must be weighed before doing so. Treatment of opioid-induced myoclonus includes opioid reduction or opioid rotation.

Medications that enhance central inhibition are used to treat myoclonus in children who have SNI. Valproic acid and clonazepam are considered first-line therapy for cortical myoclonus (Caviness 2009; Jiménez-Jiménez, Puertas, and Toledo-Heras 2004). Levetiracetam and piracetam, structurally similar, have been less studied. They can be considered as sole therapy or as add-on therapy (Caviness 2009). In addition to clonazepam, other benzodiazepines have been used. Again, it is important to balance the goal of decreasing myoclonus with the potential toxicity of treatment.

SEIZURES AND EPILEPSY

A seizure is a sudden, abnormal electrical discharge in the brain that can result in physical movements, an alteration in consciousness, or a combination of symptoms. *Epilepsy* is the term used when a person has two or more seizures that are not provoked by specific events, such as low blood glucose. *Status epilepticus* refers to continuous seizure activity or repeated seizures without full recovery of consciousness between seizures, often defined as a seizure occurring for more than 30 minutes. Injury or impairment of the CNS places a child at risk for a seizure. The focus here is on understanding treatment options, anticipating side effects associated with therapy, home care plans for prolonged seizures, and decision making about interventions for intractable epilepsy in children who have SNI.

A detailed history of an episode that suggests a seizure is the most important information for making a diagnosis. Questions that are asked include: Were there jerking movements, repetitive chewing, blinking, eye deviation? Was there a loss of consciousness? How long did the episode last? Did the child look drowsy or sleep after the episode? If possible, a video recording of an episode can be very useful. An EEG (electroencephalogram) is a test used by neurologists in the diagnosis of epilepsy. An EEG records the electrical activity of the brain, indicating normal or abnormal activity. A neurologist will review the information from the history, the video (if available), and the EEG to make a diagnosis.

When considering whether an event indicates a seizure, it is important to keep in mind other problems that can mimic seizures. For children who have SNI, these can include episodes of arching and posturing (as reviewed later), repeated muscle spasms, and exaggerated startle reactions. In general, movement that is not the result of a seizure is not followed by a postictal period (the time following a seizure when the person often has an altered level of alertness) and is typically not as rhythmic, regular, or symmetric.

It is important to consider factors that can lower the seizure threshold, such as a missed dose of an antiepileptic drug (AED), abrupt discontinuation of a benzodiazepine or AED, and starting or stopping a medication that can alter the metabolism of an AED. Medications that can lower the seizure threshold include baclofen, metoclopramide, neuroleptics, tramadol, and TCAs (Gardner et al. 2000; Koppel 2002). Other triggers include illness and fever, sleep deprivation, including obstructive sleep apnea, and pain and discomfort (Kotagal and Yardi 2008; Wusthoff, Shellhaas, and Licht 2007).

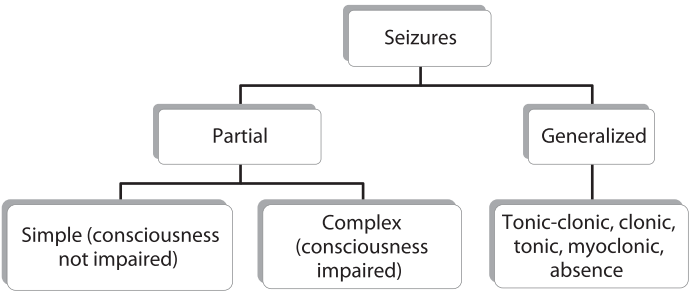


Figure 7.1. Seizure classification

Seizure types

Seizure types are first organized by whether the source of the seizure in the CNS is localized, referred to as a partial-onset seizure, or is generalized. A partial-onset seizure may generalize, in which case it is referred to as secondary generalization. Partial seizures are also divided into several types: simple partial seizures, seizures with no alteration in consciousness, and complex partial seizures, when consciousness is altered (figure 7.1).

Generalized seizures involve loss of consciousness and are classified according to the effect on the body: absence ("staring spells" without movement), myoclonic (brief, quick muscle jerks, often involving the face or arm, though they can involve the whole body), clonic (contraction and relaxation), tonic (stiffening), and tonic-clonic (the body stiffens and jerks rhythmically; also referred to as "grand mal" seizures).

In addition to muscle contractions, other features that can suggest a seizure include repetitive eye movements, tongue thrusting, oral movements such as lip smacking, and bicycling or swimming movements. Such manifestations are especially common in newborns, probably due to lack of myelin maturation. Seizure classification is used to guide the selection of medication. This classification entails a comprehensive history of all events and is commonly supplemented with information from an EEG. A neurologist is generally involved in guiding evaluation and treatment decisions.

Seizure syndromes

Seizures are also classified into seizure syndromes. Only a few are reviewed here, those that can have associated SNI (Wirrell, Farrell, and Whiting 2005).

Infantile spasms (West syndrome)

West syndrome is a triad consisting of seizures termed infantile spasms, developmental delay, and an EEG pattern of hypsarrhythmia. Features of infantile spasms include abrupt bending or flexing of the neck, trunk, and arms, along with flexion or extension of the legs. Onset typically occurs after 2 months of age, with peak onset between 4 and 8 months. Infantile spasms are classified into three types: symptomatic, when an underlying problem is identified, such as a malformation of cortical development, hypoxic-ischemic encephalopathy, or an inborn error of metabolism; cryptogenic, when no cause is identified; and idiopathic, when the cause is unknown and development was normal prior to onset. Some use the terms *cryptogenic* and *idiopathic* interchangeably. The prognosis varies with the underlying cause. In general, most patients have significant intellectual impairment and continuing seizures that may evolve to Lennox-Gastaut syndrome.

Lennox-Gastaut syndrome

This seizure syndrome is a triad consisting of multiple types of generalized seizures, cognitive impairment, and an EEG pattern of slow spike-waves. Onset most commonly begins in early childhood, with a peak onset between 2 and 8 years of age. Like West syndrome, Lennox-Gastaut syndrome either results from symptomatic (known) causes or is classified as cryptogenic or idiopathic. Approximately 20% of people who have Lennox-Gastaut syndrome have a history of West syndrome. Anticonvulsants are usually only partially successful in treatment. The long-term outcome is generally poor, with most children showing progressive intellectual deterioration with age. A poorer cognitive outcome is predicted by onset before 3 years of age and a history of West syndrome.

Dravet syndrome

In Dravet syndrome, previously known as severe myoclonic epilepsy of infancy, seizures begin in the first year of life, with normal development prior to their onset. In most cases, the first seizures occur with mild fever and are generalized tonic-clonic or unilateral seizures that may switch sides from one event to the next. These seizures are often prolonged, often leading to status epilepticus, and often resistant to antiepileptic medications. In time, seizures increase in frequency and begin to occur without

fever. Additional seizure types appear, most often including myoclonic and complex-partial seizures. Mutations in the type 1 sodium channel (SCN1A) are frequently found in people who have this condition. The course is highly variable from person to person. Additional features include autism spectrum characteristics, movement disorders, dysautonomia, and problems with growth and nutrition.

Treatment

Treatment of epilepsy includes antiepileptic drugs, ketogenic diet, vagus nerve stimulation, and surgical resection.

Antiepileptic drugs

Antiepileptic drugs, also called anticonvulsants, work by decreasing the electrical impulses of neurons in the brain, thus stopping a seizure from occurring or spreading. Treatment principles can be summarized as follows (Pellock 2002; Pellock and Morton 2000; Rutecki and Gidal 2002; Wheless et al. 2007; Wheless, Clarke, and Carpenter 2005):

- The selection of an AED is based on the identified seizure type and on the potential toxicity of the drug.
- First-line drugs for generalized tonic-clonic seizures include valproic acid and lamotrigine (the latter especially for younger children, because of the increased risk of toxicity with valproic acid in children younger than 2 years). Second-line or add-on therapy includes carbamazepine, levetiracetam, oxcarbazepine, phenytoin, topiramate, and zonisamide.
- Valproic acid is considered first-line treatment for symptomatic myoclonic seizures. Second-line or add-on therapy includes lamotrigine, levetiracetam, topiramate, and zonisamide.
- Treatment begins with one drug, with the dosage increased until the seizures stop or medication toxicity develops. If toxicity occurs before seizures are controlled, the first drug is tapered and a second single drug is started.
- If a patient fails to respond to a second medication trial, options include a third monotherapy (one drug) trial or a combination of two AEDs.
- Options with continued failure include a second combination of two AEDs, then consideration of the ketogenic diet, vagus nerve stimulation, or epilepsy surgery.

- Alterations in the dose of an AED should be made gradually, such as once every 5 to 7 days. If an anticonvulsant medication is to be discontinued, it should be discontinued gradually. Sudden discontinuation of an AED is one of the most common causes of status epilepticus.
- Monitoring blood levels of an AED is often unnecessary. Monitoring of blood cell counts and liver function is recommended for some drugs.

For children who receive drugs by feeding tubes, these practical details can be beneficial:

- AEDs available as a liquid include carbamazepine, levetiracetam, oxcarbazepine, phenobarbital, phenytoin, and valproic acid.
- Tablets generally allow more stable delivery than liquids or, especially, suspensions.
- Immediate-release tablets can be crushed, dissolved in water, and given by feeding tubes.
- Extended-release tablets or capsules should not be crushed, and sprinkle formulations will clog feeding tubes.
- AEDs without an IV formulation include carbamazepine, lamotrigine, oxcarbazepine, and topiramate.
- In general, AEDs that can be given rectally, if needed, in the short term include carbamazepine, phenobarbital, lamotrigine, and valproic acid, all given at the same dose (table 7.2) (Birnbaum et al. 2001; Epilepsy.com 2011; Graves et al. 1989; S. Smith, Sharkey, and Campbell 2001). See table 4.7 for information on giving medications rectally.

TABLE 7.2 Guidelines for giving antiepileptic drugs rectally

Medication	Comments
Carbamazepine	• Dilute oral suspension with equal volume of water • Can have a cathartic effect
Lamotrigine	• Crush chewable/dispersible or compressed tablet and mix with 6 mL of room-temperature tap water
Phenobarbital	• Use parenteral solution
Valproic acid	• Dilute oral suspension with equal volume of water • Can have a cathartic effect

Medication side effects

Side effects are common with these medications but can be minimized with the use of the smallest effective dose. It is important to anticipate the side effects associated with the AEDs (Gissel, Poulsen, and Vestergaard 2007; Jekovec-Vrhovsek, Kocijancic, and Prezelj 2000; Landmark, Johannessen, and Tomson 2012; Pellock 2002; Pellock and Morton 2000; Rutecki and Gidal 2002; Walia et al. 2004). Table 7.3 summarizes information on side effects. (See table 7.7 for a summary of the side effects associated with individual medications.)

Drug monitoring

Blood tests are sometimes used to monitor and assess for medication toxicity. Such tests can include measuring drug level (the amount of an AED in the blood) and testing for side effects such as low sodium, low white blood cell count, or liver toxicity. There is no "right" approach, though understanding some principles can minimize unnecessarily frequent blood tests.

The therapeutic range indicated for each AED is the average range identified in a sampling of individuals. The lower end of the range indicates the level above which the majority of those individuals had seizure control. The upper end of the range indicates the level below which the majority of those individuals did not have toxic effects from the drug.

For a specific child, the most important information is the dose of an AED that results in seizure control without toxicity. If a child is having seizures without toxicity, the dose of the AED can be increased, even if the blood drug level is at the upper end of the therapeutic range. On the other hand, if the drug level is at the low end of the range and the child is no longer having seizures, it might be reasonable not to increase the dose. If a child has no seizures but has a drug level above the upper limit of the range, it might be appropriate not to lower the dose, but the child needs to be closely monitored for signs of toxicity. The therapeutic range can serve as a guide, but control of seizures, on the one hand, and signs of toxicity, on the other, are indicators of the dose that is most appropriate for each child.

For these reasons, frequent, routine measures of blood levels of these drugs are not necessary. Instead, a blood level can be helpful if a child is having seizures or has a problem that might be due to drug toxicity. For a

TABLE 7.3 Side effects associated with antiepileptic drugs (AEDs)

Side effect	Medications	Comments
Sedation	Phenobarbital, phenytoin (Dilantin), valproic acid (Depakene), carbamazepine (Tegretol), topiramate (Topamax)	• Sedation can be minimized if the medication dose is increased slowly • Sedation often lessens over time
Nausea, gastrointestinal discomfort, decreased appetite	Valproic acid, carbamazepine, oxycarbazepine (Trileptal), topiramate, zonisamide (Zonegran)	• Similar to the symptoms associated with gastroesophageal reflux
Pancreatitis (inflamed pancreas)	Valproic acid	• Symptoms include pain, vomiting, feeding intolerance, and abdominal distension
Hepatotoxcity (liver damage)	Valproic acid, felbamate (Felbatol), phenytoin (rare), carbamazepine (rare)	• The risk with valproic acid is greater for children under 2 years of age and when used in combination with other medications • Symptoms include nausea, vomiting, fatigue, and jaundice (yellowing of the eyes and skin)
Agitation and irritability	Levetiracetam (Keppra), lamotrigine (Lamictal)	• Important to consider medications along with other causes of irritability
Skin rashes	Lamotrigine, carbamazepine, phenytoin, phenobarbital	• A severe skin disorder (Stevens-Johnson syndrome) can result in separation of the epidermis (outer layer of skin) from the dermis; this typically occurs within the first month of a new drug and is considered a medical emergency
Gum hyperplasia	Phenytoin	• May lessen with good oral hygiene and improves after discontinuation of the medication

(continued)

TABLE 7.3 *(continued)*

Side effect	Medications	Comments
Bone marrow suppression	Carbamazepine, possibly oxcarbazepine	• This can suppress the production of white blood cells, red blood cells, and platelets • Symptoms include easy bruising, petechiae (small red spots) on the skin, and paler skin
Aplastic anemia (lack of production of red blood cells)	Felbamate	• Requires close monitoring
Hyponatremia (low serum sodium)	Carbamazepine, oxycarbazepine	• Related to syndrome of inappropriate antidiuretic hormone (SIADH) • Unusual for serum Na^+ to be significantly lowered (<125 mEq/L)
Metabolic acidosis	Topiramate	• This can increase the risk of renal stones
Nephrolithiasis (kidney stones)	Topiramate (rate may be significantly higher in non-ambulatory children)	• Symptoms include pain, blood in urine, stones in the diaper
Decreased bone mineral density (BMD)	Carbamazepine, phenytoin, phenobarbital, valproic acid; newer AEDs not as well studied	• Supplementation with vitamin D and calcium may improve BMD
AEDs as hepatic enzyme inducers (decrease the level of a drug through increased metabolism by these enzymes)	Phenobarbital, phenytoin, carbamazepine, oxcarbazepine, topiramate (weak)	• Changes in a child after a new medication has been started or stopped should prompt consideration of altered drug metabolism
Other drug interactions	Valproic acid	• Increases the level of carbamazepine and TCAs by decreasing clearance
No alteration in the metabolism of other drugs	Levetiracetam, gabapentin	• They do not alter the metabolism of other AEDs and are not significantly altered by other AEDs

child who is having seizures, a drug level measurement can make certain that the drug is being absorbed, is not being metabolized too fast, and is being given to the child. If the child is having a problem that might be due to drug toxicity, such as increased sedation, a drug level measurement can help determine whether the problem might be from the drug or whether other causes need to be considered. Other times to obtain a blood level include at a time of optimal seizure control, so that the level can serve as a reference point in the event that seizures return or side effects occur, or when elimination of the drug may be altered, such as with renal or liver disease.

In addition to measuring antiepileptic drug levels, blood tests are also considered for assessing the specific types of side effects associated with different AEDs. The need for a blood test can be determined by the occurrence of problems that suggest possible toxicity. Though studied mostly in adults, frequent routine blood tests do not result in better treatment or outcome (Irshaid, Hamdi, and Al Homrany 2003; Kim and Berlowitz 1994; Tomson, Dahl, and Kimland 2007). A complete blood cell count (CBC) and a metabolic panel can be obtained annually when a child is taking an AED that can cause low sodium, low blood cell count, or liver toxicity. Again, obtaining blood tests at other times can be guided by the development of problems that suggest drug toxicity. An exception here is when a child is taking felbamate, which requires more frequent monitoring. Other tests can be based on the development of symptoms, such as obtaining a lipase level when a child has acute pain and vomiting. Based on the side effects with different AEDs, a parent can learn the symptoms that need to be brought to the attention of a physician (see table 7.3).

Treating a prolonged seizure

Seizures typically last from a few seconds to a few minutes. Most seizures stop within 5 minutes. Recovery following a seizure, referred to as the postictal period, may take several minutes to several hours. Most people having a seizure lasting longer than 5 minutes require medical intervention. A child who has had one prolonged seizure is at risk for having another. A medication can be prescribed to give at home when a seizure lasts longer than 5 minutes or for a cluster of seizures without recovery to baseline (Wheless, Clarke, and Carpenter 2005; Wusthoff et al. 2007). Medications include lorazepam (given buccally), midazolam (buccally or intranasally), and diazepam (rectally). There is increasing evidence that midazolam is as effective as rectal diazepam (Appleton, Macleod, and

Martland 2008; Holsti et al. 2010; McIntyre et al. 2005; Mpimbaza et al. 2008).

Status epilepticus is a constant or near-constant state of prolonged seizure, often defined as lasting more than 30 minutes. Approximately 15% to 20% of all people who have epilepsy will have at least one episode of status epilepticus (Fountain 2000). Factors that increase this risk include young age, genetic predisposition, and a history of an acquired brain insult. Status epilepticus is considered a medical emergency. A seizure action plan may recommend calling paramedics if a seizure has not stopped within 10 minutes of a benzodiazepine dose. In the hospital, a loading dose of an AED can be given. Options include phenobarbital, typically used for children younger than 1 year; fosphenytoin, used for children older than 1 year, and valproic acid (Wheless, Clarke, and Carpenter 2005). For some children with a longstanding seizure disorder, a seizure action plan may change to include a second dose of a benzodiazepine if a seizure has not stopped within 10 minutes of the first dose.

Parents are often concerned that a prolonged seizure can cause injury to the brain. This is a difficult question to study, because it is hard to differentiate the effects of the seizure from the underlying cause of the seizure, any preexisting impairment of the CNS, and the effects of AED treatment. Most studies show that CNS impairment is the cause of the seizure, rather than the seizure contributing to this impairment (Raspall-Chaure et al. 2006). Though a seizure lasting less than 30 minutes is not considered to carry a risk of causing brain damage, the goal is to stop the seizure as soon as possible.

Amy is 22 years old. She has SNI as a result of congenital cytomegalovirus. Problems associated with her SNI include severe hearing impairment, cortical visual impairment, and a seizure disorder. She receives her nutrition and fluids by a gastrostomy feeding tube and has had a fundoplication. She has taken multiple AEDs, was previously treated with the ketogenic diet, and is currently taking three AEDs.

A conflict has arisen between Amy's neurologist and her mother regarding Amy's care plan for prolonged seizures. Her mother wishes to focus on home care plans. If Amy is admitted to the hospital, her mother requests that it honor an existing order not to intubate or resuscitate. Amy's neurologist requests that she be admitted if her seizure persists despite two doses of rectal diazepam. In addition, he requests that the medical team intubate Amy if treatment of the seizure in the hospital results in respiratory failure.

A palliative care consultation results in a conversation with Amy's mother, along with members of her clinical team. Current plans include rectal diaze-

pam if a seizure lasts longer than 5 minutes, repeated 10 minutes later if needed. Amy's mother and caregivers have observed that repeated medications are more likely to result in respiratory depression than a prolonged seizure. An example is given of clusters of seizures that did not stop until 12 hours later, despite two doses of diazepam. During this time, Amy appeared comfortable with no experience of respiratory depression. She returned to her prior baseline following this event. Amy's mother and home care nurses are more concerned about the harm of "aggressive" treatment in the hospital versus taking a "watch and wait" approach.

A review of other health issues identifies that Amy is having more frequent respiratory illnesses, now occurring every 2 to 4 months. During respiratory illnesses she is noted to be in distress; she has facial grimacing and nasal flaring, and she appears agitated. There are otherwise no concerns about pain or discomfort for Amy.

A follow-up meeting is arranged for Amy's primary physician, members of her home care team, her neurologist, and a member of the palliative care team. Questions asked at the meeting include: How will treatment of seizures in the hospital improve Amy's overall seizure control? What is the likelihood that treatment will increase the risk of respiratory failure? How does this contrast with the risks associated with a prolonged seizure? Will "aggressive" treatment with medications, which can increase her risk for respiratory failure through sedation, prevent a prolonged seizure from happening again? From this discussion, detailed home care plans are considered, including a respiratory care plan for home treatment of respiratory illnesses with an antibiotic and integration of symptom management with morphine sulfate. It is determined that the goal of any hospitalization is Amy's comfort, the use of noninvasive care plans to improve health when possible, and the documentation of current orders regarding limits on resuscitation. There is agreement not to attempt too many medication trials for her seizures and to focus on home care plans as much as possible. Amy's mother is delighted with the plans and the support provided.

Managing intractable (refractory) epilepsy

Some children who have SNI develop intractable epilepsy (also called refractory epilepsy) despite multiple medication trials. People who have an inadequate response from monotherapy with three different AEDs for the correct seizure type, with adequate doses, are likely to have refractory epilepsy (Kwan and Brodie 2000; Oskoui et al. 2005). For such people, the decreasing likelihood of benefit must be weighed against the

risk of associated toxicities. The risk of intractable epilepsy in children is highest for those with multiple seizure types and with the greatest impairment (Oskoui et al. 2005). As an example, in one study, seizure control was achieved in 74% of people who had normal to borderline intelligence versus 48.7% of those with intellectual impairment (Singhi et al. 2003).

When the problem is intractable, families face the challenge of balancing the potential burden and benefit of further medication trials, other interventions, and hospitalizations. Parents can be helped with decision making, especially if they are observing changes in their child's health status in conjunction with refractory epilepsy (Berg et al. 2001; Camfield and Camfield 2007).

Ketogenic diet

The ketogenic diet is effective for some children who have seizures that are refractory to drug therapy and for some children who have a toxic reaction to drugs (Neal et al. 2008). The ketogenic diet is a rigidly controlled diet that attempts to reproduce the ketosis and acidosis of starvation by restricting protein and carbohydrate intake and supplying 80% of calories through fats. It requires a strict review of the carbohydrate content of medications. Though the biochemical mechanism of effectiveness is unknown, 30% to 60% of children on this diet have improved seizure control. The diet can be useful for treating children who have myoclonic and generalized seizures. Side effects associated with the ketogenic diet include hypoglycemia (low blood sugar), constipation, kidney stones, and gallstones.

Vagus nerve stimulator

Stimulation of the vagus nerve is another intervention for seizure management. The vagus nerve stimulator (VNS) is a battery-operated generator that is implanted below the skin on the left front chest wall. A connecting wire is run under the skin from the stimulator to an electrode that is attached to the vagus nerve through a small incision in the neck. The therapy is designed to prevent seizures by sending regular small pulses of electrical energy to the brain via the vagus nerve. After implantation, the VNS generator is programmed to deliver an appropriate dose of electrical stimulation. The current is gradually increased, typically at 1- to 2-week intervals, until the target dose is reached.

There is also the possibility of providing additional stimulation, which can be given by a caregiver, by placing or swiping a magnet over the chest where the generator is implanted. This magnetic activation of the VNS generator will stop or shorten a seizure in approximately 25% of patients with the implant.

VNS therapy may be effective against partial seizures and generalized epilepsies such as Lennox-Gastaut syndrome. Side effects associated with the vagus nerve stimulator include hoarseness, coughing, and problems with swallowing, though these problems tend to be mild and go away over time.

Surgery

The surgical options available for intractable epilepsy are more limited for children who have SNI, because for them, identifying a focus of seizures that can be surgically removed is less likely. For such children, nonspecific surgical options can be considered, including corpus callosotomy for generalized seizures, which involves severing the neural connections between the right and left halves (hemispheres) of the brain, and hemispherectomy, the removal of a portion of one hemisphere. Decisions about these surgical options are best made with trusted healthcare providers, with consideration of the risks and goals of care.

Decisions about intervention options for children who have SNI should be made in the context of the child's overall health and functional status, balancing the hope of benefit with the risk of the intervention. For children who have experienced a decline in health and function, there needs to be a realistic expectation about how much the intervention will contribute to improvement beyond a potential reduction in the frequency of seizures. As discussed in other chapters, alterations in the function of the CNS may be an indication of an irreversible deterioration of the CNS. Features that can suggest such a decline include changes in the level of alertness; increasing autonomic dysfunction, such as changes in intestinal motility and more frequent occurrence of extremities that are cool and blue, indicating changes in vascular (blood vessel) tone; development of shallow breathing (hypoventilation) or intermittent central apnea; escalating pain features; and increasing severity of arching and stiffening, indicating further loss of central inhibition.

Rachel is a 4-year-old who has refractory epilepsy. She has not improved despite multiple medication trials, the ketogenic diet, and a left hemispherectomy.

Rachel lost previously acquired motor and communication skills 6 months ago and remains unable to ambulate or communicate. She has had six hospital admissions in the past 5 months, most for recurrent bouts of pneumonia, despite placement of a gastrostomy feeding tube and Nissen fundoplication. Rachel's doctor recommends a vagus nerve stimulator for her intractable epilepsy.

Rachel's mother is concerned that more interventions will provide no long-term benefit while resulting in more admissions and discomfort for her daughter. She believes she has "lost" part of Rachel. She still hopes for improvement in Rachel's functional and health status, but she wishes to avoid further invasive procedures. Her medical team initially feels strongly that the VNS should be tried. During several meetings, the medical team, palliative care team, and Rachel's mother discuss medical options and identify the family's goals, hopes, and fears.

Rachel's care team supports her mother's decision to focus on active home treatment strategies for respiratory exacerbations. A medical and symptom management protocol is outlined, which includes an antibiotic for respiratory illnesses, morphine sulfate for respiratory distress, midazolam for agitation, and glycopyrrolate (Robinul) for secretions. The first time Rachel's caregivers use the plan, they report that Rachel appears more comfortable and interactive than she has been in months. The plan remains not to pursue placement of a VNS.

AUTONOMIC DYSFUNCTION

The autonomic nervous system regulates many involuntary functions in the body, including body temperature, heart rate, blood pressure, respiration rate, intestinal motility, urination, salivation, sweating, and the diameter of the pupils. It is divided into two systems, the sympathetic nervous system, or "fight or flight" system, and the parasympathetic nervous system, or "rest and digest" system.

Dysfunction of the autonomic nervous system, termed *dysautonomia*, is increasingly recognized in children who have neurological impairment (Park et al. 2002; Svedberg et al. 2008). Other terms used include *paroxysmal sympathetic hyperactivity* and *paroxysmal autonomic instability with dystonia.* When symptoms occur acutely, the terms *autonomic storm* or *sympathetic storm* are used. *Autonomic dysreflexia* is the term more typically used to describe autonomic dysfunction in people who have spinal cord injury above the splanchnic sympathetic outflow, commonly at or above spinal cord level T6, though T6 through T10 may be susceptible.

When autonomic dysfunction is seen in children who have SNI, it is typically a result of impairment in the areas of the CNS that regulate sympathetic outflow, specifically the hypothalamus, pons, and medulla oblongata. The hypothalamus is involved in regulating such functions as heart rate, blood pressure, body temperature, and sleep; the pons, in regulating sleep, respiration, swallowing, bladder control, eye movement, facial expressions, and secretion of saliva and tears; and the medulla oblongata, in regulating respiration, heart rate, blood pressure, swallowing, and vomiting.

Features of autonomic dysfunction

Dysfunction of the autonomic nervous system can result in multiple problems, because it alters the ability of the CNS to maintain homeostasis. Features of dysautonomia include tachycardia or bradycardia (increase or decrease in heart rate), hyperthermia or hypothermia (increase or decrease in body temperature), pallor or flushing of the face and body, cool hands and feet that might appear bluish and mottled, urinary retention, abnormal sweating, increased salivation, posturing, agitation, retching and vomiting, and bowel dysmotility and constipation. In addition, individuals able to report symptoms identify generalized discomfort and abdominal pain (Axelrod and Berlin 2009; Chelimsky and Chelimsky 2001; Chelimsky, Hupertz, and Chelimsky 1999). Children who have SNI are especially prone to increased central sympathetic outflow, resulting in symptoms of elevated heart rate and blood pressure, sweating, elevated body temperature, facial flushing, retching, agitation, arching, and stiffening.

Treatment

The goal of treatment is to minimize any distress or discomfort associated with autonomic dysfunction. Unfortunately, treatment of dysautonomia has been poorly studied in children who are neurologically impaired. Case reports, predominantly of people who have hypoxic and traumatic brain injury, demonstrate mixed results. Interventions used include clonidine, benzodiazepines, oral and intrathecal baclofen, beta blockers (such as metoprolol), bromocriptine, and morphine sulfate (Baguley 2008; Baguley et al. 2004; Diesing and Wijdicks 2006).

On the basis of case reports, cyproheptadine may be beneficial for patients with autonomic dysfunction that includes hypothermia and retching (Kloos 1995; Ruiz et al. 2003; Sheth, Barron, and Hartlage 1994). Gabapentin

was reported to benefit six patients with traumatic brain injury when symptoms of dysautonomia, agitation, and spasticity persisted despite treatment with benzodiazepines, bromocriptine, morphine, clonidine, intrathecal baclofen, and metoprolol (Baguley et al. 2007). One study found benefit from pregabalin for 13 of 15 patients with familial dysautonomia, including a decrease in nausea, retching, tachycardia, and flushing (Axelrod and Berlin 2009).

Other problems that have similar features

Treatment decisions should consider other causes of the features associated with autonomic dysfunction in children who have SNI, such as medication toxicity or withdrawal, central pain, and visceral hyperalgesia. Taking all causes into account will help guide medication selection.

Several medication toxicities have features that overlap with autonomic dysfunction, including serotonin syndrome and neuroleptic malignant syndrome (table 7.4). A general approach is to determine whether any medication was started in the weeks to months before observing the symptoms that suggest autonomic dysfunction. Sudden withdrawal of a medication

TABLE 7.4 Medication toxicities

Category	Associated features	Potential causes: partial list of drugs commonly implicated or commonly used
Serotonin syndrome	Increased heart rate and blood pressure, sweating, increased body temperature, dilated pupils, diarrhea, increased spasticity and stiffening, clonus, agitation	Selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs); other drugs, especially in combination: tramadol, fentanyl, trazodone, risperidone, linezolid, ondansetron, metoclopramide
Neuroleptic malignant syndrome	Agitation, increased movement, muscle stiffening, autonomic dysfunction, increased body temperature, decreased level of alertness	Most common: dopamine antagonists such as metoclopramide and antipsychotics (neuroleptics), including haloperidol and risperidone

TABLE 7.5 Withdrawal symptoms

Drug category	Features
Opioids	Agitation, restlessness, grimacing, inconsolable crying, disrupted sleep, hiccups, goose bumps, shivering, fever, increased heart rate and blood pressure, increased respiratory rate, vomiting, gagging, diarrhea, cramps, tears, runny nose, yawning, sweating, dilated pupils, muscle spasms, seizures
Benzodiazepines	Jitteriness, agitation, increased heart rate, muscle cramps, disrupted sleep, heightened sensitivity to light and sound
Baclofen	Agitation, confusion, hallucinations, insomnia, hyperthermia, seizures, rebound spasticity, muscle rigidity
SSRIs, SNRIs, TCAs	Agitation, irritability, disrupted sleep, GI distress, tremor, sweating

Sources: Ducharme et al. 2005; Fisher 2010; Franck, Naughton, and Winter 2004.

such as a benzodiazepine, baclofen, opioid, or clonidine can exacerbate these features (table 7.5).

Many of the characteristics of autonomic dysfunction are also seen with pain from any source, as well as with the specific features of central pain and visceral hyperalgesia. Consideration of this overlap, along with the child's history, can help guide decisions about an empirical medication trial (table 7.6).

Summary of treatment options for autonomic dysfunction

- Features that suggest autonomic dysfunction in children who have SNI include altered heart rate, altered regulation of body temperature, pallor or flushing of the face and body, cold hands and feet, urinary retention, sweating, increased salivation, posturing, agitation, retching and vomiting, and bowel dysmotility.
- Other problems to consider that have similar features include medication toxicity, medication withdrawal, and pain from any source.
- Of the medication options for autonomic dysfunction, there is good reason to consider one of the gabapentinoids (gabapentin or pregabalin) or clonidine, given their potential benefit for other problems with similar features.

TABLE 7.6 Features associated with autonomic dysfunction: other considerations

Source	Features	Treatment
Pain from any source	Pain behaviors identified in nonverbal children who have SNI: crying, grimacing, increased heart rate, sweating, agitation, arching, stiffening	• Treatment of source • Empirical pain treatment
Central pain, visceral hyperalgesia	Retching, along with the pain behaviors indicated above	• Gabapentin, tricyclic antidepressants
Dysautonomia	Flushing, sweating, retching, increased heart rate, agitation, arching, stiffening	• *Scheduled:* Gabapentin, clonidine, cyproheptadine • *Intermittent (prn):* Clonidine, morphine sulfate, benzodiazepine

- Cyproheptadine may be beneficial when the associated features include retching or hypothermia.
- The goal of selecting a scheduled medication is to decrease the severity of distress associated with these features, along with the frequency and severity of autonomic storm events.
- Autonomic storm events are often manifested by an acute onset of facial flushing, sweating, tachycardia, retching, agitation, arching, and stiffening of extremities. In addition to a scheduled medication, children with intermittent autonomic storms may benefit from intermittent clonidine, morphine, or diazepam, as needed, during episodes.
- Other benzodiazepines may be considered, such as midazolam, with a more rapid onset of action, or clonazepam, with its theoretical advantage as a pain adjuvant.
- A medication trial directed at pain should be considered when features of autonomic dysfunction persist and remain troublesome.

POSTURING AND ARCHING

Posturing is involuntary flexion (bending) or extension (straightening) of the extremities, often with associated arching. The terms *decorticate*, *decerebrate*, and *opisthotonos* are used to describe specific types of posturing

noted on the clinical exam. Common problems seen in children who have SNI are abnormal posturing and arching from hypertonia, dystonic reactions from dopamine antagonists (such as metoclopramide, haloperidol, and risperidone), autonomic dysfunction, pain from any cause, and Sandifer syndrome associated with gastroesophageal reflux disease. Identifying abnormal posture and arching in children who have SNI involves considering all of these problems.

In children who have SNI, posturing can indicate a significant loss of inhibitory control by the CNS. Posturing can become progressive in children with neurodegenerative conditions. The clinical findings can include decorticate posturing, as indicated by rigid extension of the arms and legs, downward pointing of the toes, and backward arching of the head; decerebrate posturing, with rigidity, bending (flexion) of the arms, clenched fists, and extended legs; and opisthotonos, with rigidity and severe arching of the back, with the head thrown backward. Overall, these findings indicate severe impairment with loss of central inhibition of muscle tone.

Increasing frequency and severity of these clinical features warrants an investigation of other problems with similar features. Triggers such as pain should be minimized and treated, including empirical medication trials for pain. As with other problems encountered in children who have SNI, a balance must be struck when pursuing causes and empirical treatment trials, and caregivers must keep in mind that the clinical features can indicate further irreversible decline in the function of the CNS.

AGITATION, DELIRIUM, AND BEHAVIORAL CHANGES

Changes in behaviors from a child's baseline can be challenging to assess in children who have SNI. A child may appear agitated, display self-injurious behaviors, or develop other disruptive behaviors. Such behaviors can accompany disease progression, especially with inborn errors of metabolism that involve the gray matter, with resulting development of dementia. Assessing agitation, like assessing pain, in nonverbal children who have SNI can be very challenging.

Agitation is considered an unpleasant state of arousal, manifesting as irritability, restlessness, and increased motor activity. Features may include loud speech, crying, increased motor activity, increased autonomic arousal such as sweating and increased heart rate, inability to relax, and disturbed sleep-rest pattern (Wusthoff, Shellhaas, and Licht 2007). As with the other problems reviewed in this chapter, agitation can be triggered by medication toxicity, pain, stress, and illness.

In nonverbal children who have SNI, it is difficult to distinguish delirium as the cause of these changes, though this is not a critical distinction, because the causes of delirium are similar to the triggers of agitation. Delirium is a disturbance of consciousness with an acute onset, over hours to days, and a fluctuating course. Features described in adults include disordered thinking, change in cognition, inattention, altered sleep-wake cycle, perceptual disturbances, and psychomotor disturbances (Del Fabbro, Dalal, and Bruera 2006). Causes include pain, medications such as anticholinergics and benzodiazepines, and metabolic disturbances, including infection, electrolyte imbalance, renal impairment, and liver failure.

Managing agitation and delirium involves evaluating the child for treatable causes, including sources of discomfort such as pain, dyspnea, and muscle spasms. It is appropriate to consider an empirical medication trial for pain, as agitation, disruptive behaviors, and self-injurious behaviors can be manifestations of pain (Hadden and von Baeyer 2002). This relationship has mostly been studied in adults with dementia, with pain in some adults manifesting as confusion, change in behaviors, aggression, and agitation (Herr, Bjoro, and Decker 2006).

It is also important to consider conditions that mimic the appearance of agitation, such as akathisia (an unpleasant sensation of inner restlessness) caused by dopamine antagonists, SSRIs, and TCAs; withdrawal from opioids, benzodiazepines, and baclofen; and paradoxical reactions to benzodiazepines, antihistamines, and anticholinergics.

Medication options for managing agitation and delirium in children who have SNI include empirical pain treatment and neuroleptics such as risperidone. When considering an empirical treatment trial for agitation, the potential risk and benefit of different medications should be kept in mind.

Alison is a 10-year-old girl with a degenerative metabolic condition. Features of this disease include seizures, visual loss, anxiety, depression, aggressive behaviors, and psychotic disorders. Alison has many of these problems, including epilepsy, visual loss, anxiety disorder, and dementia with impaired memory and learning. She has persistent behavioral outbursts that include biting others and herself and disrupted sleep, despite trials of sertraline, alprazolam, fluoxetine, risperidone, and quetiapine. She is described as not being able to control her actions, often stating "I'm sorry" and "I can't help it" after an outburst. On "good" days, Alison is happy, joking, "a pleasure to be around." Unfortunately, these days have become less frequent.

Her family and caregivers have thought that these outbursts are a result of her disease. A pain history identifies that Alison will occasionally state "I hurt,"

though she does not indicate where. She is taking tramadol, which provides some benefit, though it is insufficient at night. Other current medications include quetiapine, citalopram, valproic acid, and levetiracetam (Keppra). Pain as a contributing source to her behaviors is considered. Gabapentin is initiated, resulting in a 30% to 40% improvement in Alison's behaviors and sleep. Nortriptyline is added, with significant improvement. She is described as "the best she has been in years." Her parents report that "she hasn't made a hole in the wall since she has been on this dose," and that the result is "too good to be true." The overall focus of Alison's care has shifted to providing comfort.

ALTERATIONS IN AROUSAL AND ALERTNESS

Assessing the causes of change in a child's level of alertness starts with considering medication toxicity and acute illness, including reviewing any medications recently started or stopped that could result in toxicity or alter the metabolism of other medications.

When change in alertness occurs intermittently, with no identifiable cause, one possibility is alterations in the areas of the CNS that regulate arousal and sleep. These areas include the hypothalamus and pathways in the thalamus. This is covered in greater detail in chapter 8.

DECLINING FUNCTION OF THE CENTRAL NERVOUS SYSTEM

Various explanations are possible for any problem that can potentially indicate an alteration in the function of the CNS. Sources to consider when a new problem such as sedation or apnea develops include acute illness, medication toxicity, disease progression involving the CNS, and the effects of anesthesia for surgical or other procedures. When one problem occurs that might be under the regulation of the CNS, and with no identified cause, it is helpful to look for the presence of other features that are also regulated by the CNS. The presence of multiple changes with no cause, as identified for Jonathan as described below, suggests an irreversible decline of the CNS.

Other features to look for when one change is noted include decreased arousal, increased sleeping, altered breathing pattern including intermittent brief pauses, lower heart rate, decreased body temperature, cool hands and feet that are mottled or blue, and slowing of intestinal function that may be noted as increasing feeding intolerance. When only one change is noted, it is typically not significant. For example, the heart rate may become slower over time, especially when sleeping, as the metabolic

needs of the child decline. In addition, some changes are initially intermittent and transient, perhaps over months or years. Some problems can become persistent with a new plateau noted, again, occurring over months or years. As the decline becomes more significant and critical, these features may be seen more frequently and for longer periods of time, and new features may be identified. The identification of multiple problems that can suggest an irreversible decline of the CNS may reflect ongoing apoptosis (cell death) or lack of regeneration of neurons in the areas of the brain that regulate heart rate and other vital body functions.

Jonathan is a 14-year-old boy who has SNI as a result of birth asphyxia. His medical history includes a seizure disorder, use of a feeding tube for all fluids and nutrition, intrathecal baclofen pump, and a tracheostomy tube with home mechanical ventilation. He is being assessed following two hospitalizations in the past month as a result of changes in his level of alertness. He is difficult to arouse, has a decrease in heart rate to the 40s, and has a decrease in respiratory effort, with oxygen saturation in the mid- to high 90s. Assessment does not disclose any clear reasons for the changes observed.

These changes are new for Jonathan over the past 2 months. He has been sleeping more and has episodes of a lower heart rate, in the 40s, compared with his previous baseline in the 70s when sleeping. He is also noticed to have colder hands and feet over the past several months, and they can appear purple and puffy at times. These changes in his extremities do not correlate with his heart rate. One family member states, "This might be the reality of Jonathan's new baseline." The family also notes that Jonathan has "not been the same" since a family member involved in his daily care died, 11 months ago.

Discomfort is also identified as a concern. Most recently, Jonathan has developed persistent pain since a urinary tract infection 3 months ago. The pain appears to be localized to his abdomen and increases before a bowel movement and flatus. Jonathan has also been experiencing more feeding intolerance. All evaluations have produced negative findings, including blood and urine tests and abdominal CT scan. When uncomfortable, Jonathan develops a significant increase in clonus and muscle spasms.

A lengthy discussion identifies the hopes, worries, and goals of the family. In this discussion, there is acknowledgement that the clinical changes in alertness, heart rate, respiratory effort, circulation, and discomfort may reflect a decline in the function of Jonathan's brain. There is general agreement from all family members that this is probably the best explanation for the ongoing problems, given that all test results have been negative and that there is no improvement despite alterations in some of his sedating medications.

TAKE-HOME POINTS

- Table 7.7 summarizes the mechanisms, uses, and side effects of the medications used for treating problems of the central nervous system, as described in this chapter.
- The problems of the CNS, including spasticity, dystonia, seizures, and autonomic dysfunction, can be triggered and worsened by pain.
- A thorough review of potential pain sources should be done; some children will have improvement in problems of the CNS with an empirical medication trial for pain sources, such as central neuropathic pain and visceral hyperalgesia (see chapter 4).
- Other contributing factors should be maximally addressed, including bowel management and sleep pattern.
- Other comfort strategies include cuddling, positioning, massage, a cool fan, vibrating mats, and weighted blankets.
- Though spasticity is typically not painful, associated intermittent muscle spasms often are painful.
- Of the medications available for spasticity, alpha-2 receptor agonists (clonidine and tizanidine) and gabapentin may have an added advantage, given their potential for also treating pain.
- Diazepam may be best used as an intermittent, as-needed medication for prolonged painful spasms.
- Intrathecal baclofen is beneficial for treating both spasticity and dystonia of central origin, though the potential benefit must be weighed against the associated complications.
- Botulinum toxin (Botox) is beneficial for localized spasticity management.
- Seizure triggers include medications (baclofen, neuroleptics, tramadol, and tricyclic antidepressants), missed doses or sudden withdrawal of an antiepileptic drug, illness and fever, sleep deprivation, stress, pain, and discomfort.
- A trial of multiple antiepileptic medications must weigh the diminishing benefit against the risk of medication toxicity, especially when using several medications simultaneously.
- Features associated with autonomic dysfunction are also seen with pain from any source, central pain / visceral hyperalgesia, and certain medication toxicities (serotonin syndrome and neuroleptic malignant syndrome).

TABLE 7.7 Medications used for treatment of neurological problems

Medications	Mechanism of action	Comments
Spasticity and muscle spasms		
Diazepam (Valium)	Potentiates GABA, an inhibitory neurotransmitter	• Diazepam best used in the short term for spasticity (2–4 weeks) or intermittently for muscle spasms • Other benzodiazepines can also be beneficial for treating intermittent muscle spasms
Clonidine (Catapres) Tizanidine (Zanaflex)	Centrally acting alpha-2 adrenergic receptor agonist, reducing sympathetic outflow ("fight or flight")	• Tizanidine studied more than clonidine, though less information in children • Clonidine has the advantage of delivery options (liquid and patch) and potential benefit for dysautonomia • Clonidine transdermal patch can be used after oral dose is determined (0.1 mg/24 hr, 0.2 mg/24 hr, 0.3 mg/24 hr) • Both have possible antinociceptive effects • Do not stop abruptly; must be tapered
Gabapentin (Neurontin)	Thought to inhibit excitation in the CNS	• Gabapentin is also effective for central pain and dysautonomia • No known drug-drug interactions
Baclofen	Modulates $GABA_B$ receptors	• Baclofen available only orally; sudden discontinuation can result in severe withdrawal symptoms
Dysautonomia		
Gabapentin (Neurontin)	See above	• The goal with scheduled medications (gabapentin, clonidine, cyproheptadine) is to decrease frequency, duration, and severity of autonomic symptoms and "autonomic storm" episodes
Pregabalin (Lyrica)	Same as gabapentin	
Clonidine (Catapres)	See above	

TABLE 7.7 *(continued)*

Medications	Mechanism of action	Comments
Cyproheptadine (Periactin)	5HT-2, H-1, and Ach receptor antagonist	• The goal with intermittent (prn) medications (clonidine, morphine, benzodiazepine) is to lessen the duration and severity of an "autonomic storm" episode • Scheduled gabapentin may have greater benefit when features include discomfort, agitation, stiffening, and intermittent spasms • Cyproheptadine may have greater benefit when features include hypothermia and/or retching • Benzodiazepines include clonazepam (Klonopin) diazepam (Valium), lorazepam (Ativan), midazolam (Versed)
Propranolol or metoprolol	Beta blockers	
Morphine	CNS opioid receptors	
Benzodiazepines	Potentiates GABA by increased affinity for $GABA_A$ receptors	
Dystonia and chorea		
Trihexyphenidyl (Artane)	Anticholinergic (M_1 muscarinic receptor blocker)	• Anticholinergic side effects of trihexyphenidyl may be managed with pyridostigmine • Tetrabenazine used to treat chorea associated with Huntington disease
Tetrabenazine	Dopamine depletor	
Myoclonus		
Clonazepam (Klonopin)	See diazepam	• Tolerance develops with chronic use • Used for myoclonic seizures
Seizures: acute home therapy for prolonged seizure or cluster of seizures		
Benzodiazepines	See above	• Delivery options: diazepam (Valium)—rectal; lorazepam (Ativan)—buccal, IV, or rectal; midazolam (Versed)—buccal, intranasal, or IV

(continued)

TABLE 7.7 *(continued)*

Medications	Mechanism of action	Comments
Seizures: chronic therapy		
Carbamazepine (Tegretol)	Inhibits sodium (Na^+) channel currents	• Side effects include sedation, nausea, rash, bone marrow suppression, low serum sodium, hepatotoxicity • Associated with decreased bone mineral density (BMD) • Increases the metabolism of other medications
Lamotrigine (Lamictal)	Inhibits Na^+ channel currents	• Side effects include agitation, nausea, rash, Stevens-Johnson syndrome
Levetiracetam (Keppra)	Unknown	• Side effects include sedation, paradoxical agitation and irritability, nausea • No interactions with other drugs
Oxcarbazepine (Trileptal)	Inhibits Na^+ channel currents	• Side effects include sedation, nausea, bone marrow suppression, low serum sodium • Associated with decreased BMD • Increases the metabolism of other medications
Phenobarbital	Enhances inhibitory action of GABA, inhibits excitatory action of glutamate	• Side effects include sedation, paradoxical irritability, rash, hepatotoxicity • Associated with decreased BMD • Increases the metabolism of other medications
Phenytoin (Dilantin)	Inhibits Na^+ channel currents	• Side effects include sedation, nausea, hepatotoxicity, rash, gum hyperplasia (overgrowth of the gums), excess body hair • Associated with decreased BMD • Increases the metabolism of other medications

TABLE 7.7 *(continued)*

Medications	Mechanism of action	Comments
Rufinamide (Banzel)	Unknown	• Side effects include sedation, nausea, irritability
Topiramate (Topamax)	May inhibit Na^+ channel currents, enhance GABA, inhibit glutamate	• Side effects include sedation, nausea, metabolic acidosis (lower blood pH), glaucoma (increased eye pressure), nephrolithiasis (kidney stones)
Valproic acid (Depakene, Depakote)	Enhances inhibitory action of GABA, inhibits Na^+ channels	• Side effects include sedation, nausea, low platelet count, pancreatitis, hepatotoxicity • Associated with decreased BMD
Zonisamide (Zonegran)	Inhibits Na^+ channels and calcium channels	• Side effects include sedation, nausea, irritability

Note: GABA (gamma-aminobutyric acid) is an inhibitory neurotransmitter involved in regulating neuronal excitability; glutamate is an excitatory neurotransmitter; agonists stimulate the receptor, antagonists block the receptor.
Abbreviations: 5HT, serotonin; Ach, acetylcholine; H-1, histamine.

- Of the medications available for autonomic dysfunction, a gabapentinoid (gabapentin or pregabalin) and/or clonidine may have the greatest benefit for children who have SNI, given the overlap in the features of autonomic dysfunction and pain.
- Cyproheptadine may be beneficial for children who have dysautonomia and associated retching and hypothermia.
- Intermittent autonomic storms may benefit from as-needed clonidine, morphine, or diazepam, along with a scheduled medication given regularly, such as clonidine or gabapentin.
- Severe posturing, arching, and stiffening in children who have SNI often reflect a significant loss of central inhibition of muscle tone.
- When problems become persistent and intractable, consideration of further treatment trials should balance the risk of treatment and the extent to which such treatment assists with improving comfort and other identified goals.

References

Albright AL, Barron W, Fasick M, et al. 1993. Continuous intrathecal baclofen infusion for spasticity of cerebral origin. *JAMA* 270(20): 2475–77.

Albright AL, Barry M, Fasick P, et al. 1996. Continuous intrathecal baclofen infusion for symptomatic generalized dystonia. *Neurosurgery* 38(5): 934–39.

Albright AL, Barry MJ, Shafton DH, Ferson SS. 2001. Intrathecal baclofen for generalized dystonia. *Dev Med Child Neurol* 43(10):652–57.

Albright AL, Gilmartin R, Swift D, et al. 2003. Long-term intrathecal baclofen therapy for severe spasticity of cerebral origin. *J Neurosurg* 98(2):291–95.

Appleton R, Macleod S, Martland T. 2008. Drug management for acute tonic-clonic convulsions including convulsive status epilepticus in children. *Cochrane Database Syst Rev* (3):CD001905.

Axelrod FB, Berlin D. 2009. Pregabalin: a new approach to treatment of the dysautonomic crisis. *Pediatrics* 124(2):743–46.

Baguley IJ. 2008. Autonomic complications following central nervous system injury. *Semin Neurol* 28(5):716–25.

Baguley IJ, Cameron ID, Green AM, et al. 2004. Pharmacological management of dysautonomia following traumatic brain injury. *Brain Inj* 18(5):409–17.

Baguley IJ, Heriseanu RE, Gurka JA, et al. 2007. Gabapentin in the management of dysautonomia following severe traumatic brain injury: a case series. *J Neurol Neurosurg Psychiatry* 78(5):539–41.

Berg AT, Shinnar S, Levy SR, et al. 2001. Early development of intractable epilepsy in children: a prospective study. *Neurology* 56(11):1445–52.

Birnbaum AK, Kriel RL, Im Y, Remmel RP. 2001. Relative bioavailability of lamotrigine chewable dispersible tablets administered rectally. *Pharmacotherapy* 21(2):158–62.

Bressman SB. 2000. Dystonia update. *Clin Neuropharmacol* 23(5):239–51.

Camfield P, Camfield C. 2007. Long-term prognosis for symptomatic (secondarily) generalized epilepsies: a population-based study. *Epilepsia* 48(6):1128–32.

Caviness JN. 2009. Pathophysiology and treatment of myoclonus. *Neurol Clin* 27(3):757–77.

Chelimsky G, Chelimsky T. 2001. Familial association of autonomic and gastrointestinal symptoms. *Clin Auton Res* 11(6):383–86.

Chelimsky G, Hupertz VF, Chelimsky TC. 1999. Abdominal pain as the presenting symptom of autonomic dysfunction in a child. *Clin Pediatr (Phila)* 38(12):725–29.

Chu ML, Sala DA, Weiner HL. 2001. Intrathecal baclofen in X-linked adrenoleukodystrophy. *Pediatr Neurol* 24:156–58.

Cutter N, Scott DD, Johnson JC, Whiteneck G. 2000. Gabapentin effect on spasticity in multiple sclerosis: a placebo-controlled, randomized trial. *Arch Phys Med Rehabil* 81(2): 164–69.

Del Fabbro E, Dalal S, Bruera E. 2006. Symptom control in palliative care, part III: dyspnea and delirium. *J Palliat Med* 9(2):422–36.

Delgado MR, Hirtz D, Alsen M, et al. 2010. Practice parameter—pharmacologic treatment of spasticity in children and adolescents with cerebral palsy (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. *Neurology* 74(4):336–43.

Diesing TS, Wijdicks EF. 2006. Arc de cercle and dysautonomia from anoxic injury. *Mov Disord* 21(6):868–69.

Ducharme C, Carnevale FA, Clermont MS, Shea S. 2005. A prospective study of adverse reactions to the weaning of opioids and benzodiazepines among critically ill children. *Intensive Crit Care Nurs* 21(3):179–86.

Epilepsy.com. 2011. AEDs for rectal administration. http://professionals.epilepsy.com/page/table_procedures_rectal.html.

Fisher D. 2010. Opioid tapering in children: a review of the literature. *AACN Adv Crit Care* 21(2):139–45.

Fountain NB. 2000. Status epilepticus: risk factors and complications. *Epilepsia* 41(Suppl 2):S23–30.

Franck LS, Naughton I, Winter I. 2004. Opioid and benzodiazepine withdrawal symptoms in paediatric intensive care patients. *Intensive Crit Care Nurs* 20(6):344–51.

Gardner JS, Blough D, Drinkard CR, et al. 2000. Tramadol and seizures: a surveillance study in a managed care population. *Pharmacotherapy* 20(12):1423–31.

Gissel T, Poulsen CS, Vestergaard P. 2007. Adverse effects of antiepileptic drugs on bone mineral density in children. *Expert Opin Drug Saf* 6(3):267–78.

Graves NM, Holmes GB, Kriel RL, et al. 1989. Relative bioavailability of rectally administered phenobarbital sodium parenteral solution. *DICP* 23(7–8):565–68.

Hadden KL, von Baeyer CL. 2002. Pain in children with cerebral palsy: common triggers and expressive behaviors. *Pain* 99(1–2):281–88.

Henney HR 3rd, Chez M. 2009. Pediatric safety of tizanidine: clinical adverse event database and retrospective chart assessment. *Paediatr Drugs* 11(6):397–406.

Herr K, Bjoro K, Decker S. 2006. Tools for assessment of pain in nonverbal older adults with dementia: a state-of-the-science review. *J Pain Symptom Manage* 31(2):170–92.

Holsti M, Dudley N, Schunk J, et al. 2010. Intranasal midazolam vs rectal diazepam for the home treatment of acute seizures in pediatric patients with epilepsy. *Arch Pediatr Adolesc Med* 164(8):747–53.

Hoving MA, van Raak EP, Spincemaille GH, et al. 2009. Safety and one-year efficacy of intrathecal baclofen therapy in children with intractable spastic cerebral palsy. *Eur J Paediatr Neurol* 13:247–56.

Irshaid YM, Hamdi AA, Al Homrany M. 2003. Evaluation of therapeutic drug monitoring of antiepileptic drugs. *Int J Clin Pharmacol Ther* 41(3):126–31.

Jankovic J. 2009. Treatment of hyperkinetic movement disorders. *Lancet Neurol* 8(9): 844–56.

Jekovec-Vrhovsek M, Kocijancic A, Prezelj J. 2000. Effect of vitamin D and calcium on bone mineral density in children with CP and epilepsy in full-time care. *Dev Med Child Neurol* 42(6):403–5.

Jiménez-Jiménez FJ, Puertas I, de Toledo-Heras M. 2004. Drug-induced myoclonus: frequency, mechanisms and management. *CNS Drugs* 18(2):93–104.

Kim DE, Berlowitz DR. 1994. The limited value of routine laboratory assessments in severely impaired nursing home residents. *JAMA* 272(18):1447–52.

Kloos RT. 1995. Spontaneous periodic hypothermia. *Medicine (Baltimore)* 74(5):268–80.

Koppel BS. 2002. Contribution of drugs and drug interactions (prescribed, over the counter, and illicit) to seizures and epilepsy. In *Managing Epilepsy and Co-existing Disorders*, ed. Ettinger AB, Devinsky O, pp. 155–73. Boston: Butterworth-Heinemann.

Kotagal P, Yardi N. 2008. The relationship between sleep and epilepsy. *Semin Pediatr Neurol* 15(2):42–49.

Krach LE. 2001. Pharmacotherapy of spasticity: oral medications and intrathecal baclofen. *J Child Neurol* 16(1):31–36.

Kupsch A, Kuehn A, Klaffke S, et al. 2003. Deep brain stimulation in dystonia. *J Neurol* 250(1):147–52.

Kwan RP, Brodie MJ. 2000. Early identification of refractory epilepsy. *N Engl J Med* 342(5):314–19.

Landmark CJ, Johannessen SI, Tomson T. 2012. Host factors affecting antiepileptic drug delivery: pharmacokinetic variability. *Adv Drug Deliv Rev* 64(10):896–910.

Leo RJ, Baer D. 2005. Delirium associated with baclofen withdrawal: a review of common presentations and management strategies. *Psychosomatics* 46(6):503–7.

Lubsch L, Habersang R, Haase M, Luedtke S. 2006. Oral baclofen and clonidine for treatment of spasticity in children. *J Child Neurol* 21(12):1090–92.

Lundy C, Lumsden D, Fairhurst C. 2009. Treating complex movement disorders in children with cerebral palsy. *Ulster Med J* 78(3):157–63.

Lundy CT, Doherty GM, Fairhurst CB. 2009. Botulinum toxin type A injections can be an effective treatment for pain in children with hip spasms and cerebral palsy. *Dev Med Child Neurol* 51(9):705–10.

Mariotti P, Fasano A, Contarino MF, et al. 2007. Management of status dystonicus: our experience and review of the literature. *Mov Disord* 22(7):963–68.

McIntyre J, Robertson S, Norris E, et al. 2005. Safety and efficacy of buccal midazolam versus rectal diazepam for emergency treatment of seizures in children: a randomised controlled trial. *Lancet* 366(9481):205–10.

Mink JW, Zinner SH. 2010. Movement disorders II: chorea, dystonia, myoclonus, and tremor. *Pediatr Rev* 31(7):287–94.

Montané E, Vallano A, Laporte JR. 2004. Oral antispastic drugs in nonprogressive neurologic diseases: a systematic review. *Neurology* 63(8):1357–63.

Mpimbaza A, Ndeezi G, Staedke S, et al. 2008. Comparison of buccal midazolam with rectal diazepam in the treatment of prolonged seizures in Ugandan children: a randomized clinical trial. *Pediatrics* 121(1):e58–64.

Neal EG, Chaffe H, Schwartz RH, et al. 2008. The ketogenic diet for the treatment of childhood epilepsy: a randomised controlled trial. *Lancet Neurol* 7(6):500–506.

Oskoui M, Webster RI, Zhang X, et al. 2005. Factors predictive of outcome in childhood epilepsy. *J Child Neurol* 20(11):898–904.

Park ES, Park CI, Cho SR, et al. 2002. Assessment of autonomic nervous system with analysis of heart rate variability in children with spastic cerebral palsy. *Yonsei Med J* 43(1): 65–72.

Pellock JM. 2002. Treatment considerations: traditional antiepileptic drugs. *Epilepsy Behav* 3(6S1):18–23.

Pellock JM, Morton LD. 2000. Treatment of epilepsy in the multiply handicapped. *Ment Retard Dev Disabil Res Rev* 6(4):309–23.

Raspall-Chaure M, Chin RF, Neville BG, Scott RC. 2006. Outcome of paediatric convulsive status epilepticus: a systematic review. *Lancet Neurol* 5(9):769–79.

Rivard PF, Nugent AC, Symons FJ. 2009. Parent-proxy ratings of pain before and after botulinum toxin type A treatment for children with spasticity and cerebral palsy. *Clin J Pain* 25:413–17.

Ruiz C, Gener B, Garaizar C, Prats JM. 2003. Episodic spontaneous hypothermia: a periodic childhood syndrome. *Pediatr Neurol* 28(4):304–6.

Rutecki PA, Gidal BE. 2002. Antiepileptic drug treatment in the developmentally disabled: treatment considerations with the newer antiepileptic drugs. *Epilepsy Behav* 3(6S1): 24–31.

Sanger TD, Chen D, Fehlings DL, et al. 2010. Definition and classification of hyperkinetic movements in childhood. *Mov Disord* 25(11):1538–49.

Sanger TD, Delgado MR, Gaebler-Spira D, et al. 2003. Classification and definition of disorders causing hypertonia in childhood. *Pediatrics* 111(1):e89–97.

Semenchuk MR, Sherman S. 2000. Effectiveness of tizanidine in neuropathic pain: an open-label study. *J Pain* 1(4):285–92.

Sgouros S. 2007. Surgical management of spasticity of cerebral origin in children. *Acta Neurochir Suppl* 97(Pt 1):193–203.

Sheth RD, Barron TF, Hartlage PL. 1994. Episodic spontaneous hypothermia with hyperhidrosis: implications for pathogenesis. *Pediatr Neurol* 10(1):58–60.

Singhi P, Jagirdar S, Khandelwal N, Malhi P. 2003. Epilepsy in children with cerebral palsy. *J Child Neurol* 18(3):174–79.

Smith H, Elliott J. 2001. Alpha2 receptors and agonists in pain management. *Curr Opin Anaesthesiol* 14:513–18.

Smith S, Sharkey I, Campbell D. 2001. Guidelines for rectal administration of anticonvulsant medication in children. *Paediatr Perinat Drug Ther* 4(4):140–47.

Svedberg LE, Englund E, Malker H, Stener-Victorin E. 2008. Parental perception of cold extremities and other accompanying symptoms in children with cerebral palsy. *Eur J Paediatr Neurol* 12(2):89–96.

Tomson T, Dahl ML, Kimland E. 2007. Therapeutic monitoring of antiepileptic drugs for epilepsy. *Cochrane Database Syst Rev* (1):CD002216.

Walia KS, Khan EA, Ko DH, et al. 2004. Side effects of antiepileptics: a review. *Pain Pract* 4(3):194–203.

Watemberg N, Leshner RL, Armstrong BA, Lerman-Sagie T. 2000. Acute pediatric rhabdomyolysis. *J Child Neurol* 15(4):222–27.

Wheless JW, Clarke DF, Arzimanoglou A, Carpenter D. 2007. Treatment of pediatric epilepsy: European expert opinion, 2007. *Epileptic Disord* 9(4):353–412.

Wheless JW, Clarke DF, Carpenter D. 2005. Treatment of pediatric epilepsy: expert opinion, 2005. *J Child Neurol* 20(Suppl 1):S1–56.

Wirrell E, Farrell K, Whiting S. 2005. The epileptic encephalopathies of infancy and childhood. *Can J Neurol Sci* 32(4):409–18.

Wusthoff CJ, Shellhaas RA, Licht DJ. 2007. Management of common neurologic symptoms in pediatric palliative care: seizures, agitation, and spasticity. *Pediatr Clin North Am* 54(5):709–33.

Zuckerbraun NS, Ferson SS, Albright AL, Vogeley E. 2004. Intrathecal baclofen withdrawal: emergent recognition and management. *Pediatr Emerg Care* 20(11):759–64.

CHAPTER 8

Changes from the Expected

Sleep, Temperature, Heart Rate, Sodium Levels, Puberty, Growth, and Nutrition

Happiness is not a matter of intensity but of balance, order, rhythm and harmony.
—Thomas Merton

The ability of the body to maintain its internal environment is called homeostasis. This ability is altered in many children with severe neurological impairment. Body temperature may be different, for example. Heart rate, energy metabolism, fluid and sodium balance, onset of puberty, and sleep can also be affected.

These changes are often a source of distress for families, who worry whether the altered heart rate is life-threatening, whether the low sodium is dangerous, whether the elevated temperature is the result of an infection, and so on. It can also be distressing when a family observes signs of puberty in a child before the expected age of puberty. And along with these worries, many families also face the challenge of their child's disrupted sleep and its effect on the family. This chapter explains each problem in detail and includes strategies for managing each, as well as providing reassurance when appropriate.

WHY THESE CHANGES OCCUR IN CHILDREN WHO HAVE SNI

Alterations in homeostasis that occur in children who have SNI are a result of impairment in the areas of the brain responsible for regulating homeostasis. The primary area is the hypothalamus and closely linked structures of the central nervous system.

The hypothalamus is involved in regulating many functions of the body, including heart rate, blood pressure, vascular tone (the narrowing or

dilation of small blood vessels), sweating, body temperature, and sleep-wake cycles. This regulation occurs through control of the autonomic nervous system. In addition, the hypothalamus helps link the endocrine system with the nervous system, through several hormones released by the hypothalamus, including those involved in the following functions:

- Regulation of water and sodium balance (antidiuretic hormone, ADH; also called arginine vasopressin, AVP)
- Release of corticosteroid from the adrenal gland (corticotropin-releasing hormone, CRH)
- Thyroid function (thyrotropin-releasing hormone, TRH)
- Pubertal development (growth hormone–releasing hormone, GHRH)
- Regulation of growth (GHRH)

SLEEP DISRUPTION AND ALTERATION

Children who have SNI are at significant risk for changes in their sleep pattern, including difficulties with falling asleep, trouble staying asleep, and early-morning awakening. The prevalence of sleep disorders in this population has been reported to be as high as 75% (Jan et al. 2008). Sleep disruption can have a profoundly adverse effect on both children and members of the family, including daytime drowsiness, headaches, depression, and work-related problems (Kohrman and Carney 2000). Lack of restful sleep can affect learning, memory, attention, abstract reasoning, and other cognitive functions (Jan et al. 2008). There is also growing recognition of the impact of pain on sleep disturbance, and vice versa: pain interferes with sleep, and sleep disturbances exacerbate pain symptoms for many children who have SNI (Long, Krishnamurthy, and Palermo 2008).

Causes of disrupted sleep

Changes in sleep can result from dysfunction of the systems in the brain that are involved in sleep-wake regulation (Jan et al. 2008). This regulation involves pathways that produce cortical arousal (when the brain is awake), pathways that inhibit this arousal, and the body's biological "clock." The review presented here highlights a few components of this regulation (Saper, Scammell, and Lu 2005; Schwartz and Roth 2008).

Alertness and associated cortical arousal are mediated by several ascending pathways, which project from the upper brain stem. One pathway

innervates the thalamus, another extends into the posterior hypothalamus and forebrain. These ascending pathways are regulated by neurons in the brain area known as the ventrolateral preoptic nucleus (VLPO). The VLPO plays a central role in quieting the ascending arousal system during sleep. The neurotransmitters in this process include GABA (gamma-aminobutyric acid), an inhibitory neurotransmitter involved in regulating neuronal excitability. The interactions between the VLPO and the branches of the ascending arousal pathway serve to inhibit each other, functioning like an electrical on-off switch. The body's biological clock, also referred to as circadian rhythms, regulates the daily cycles of sleep and wakefulness. This process involves regulation from the suprachiasmatic nucleus (SCN), located in the hypothalamus. The SCN sends signals to several areas of the CNS, including the pineal gland, the area of the brain responsible for production of the hormone melatonin. The pineal gland responds to light-induced signals that shut off the production of melatonin; increased production of the hormone after dark results in a person feeling drowsy. The SCN also coordinates other body functions with the sleep-wake cycle, including temperature, blood pressure regulation, appetite, and alertness.

Impairment of any of these components can alter sleep-wake cycles. As an example, children who have midline structural malformations of the brain, such as holoprosencephaly, are at high risk for sleep disorders, because the SCN and pineal gland are located in the midline of the brain. Children who have severe maldevelopment of the cerebrum, such as hydranencephaly, can also have profound sleep disturbances, because the cerebral hemispheres contribute to sleep-wake cycles. Children who have severe visual impairment can experience disruption of sleep because of the inability to detect light-dark cycles.

Other problems experienced by children who have SNI can also interfere with sleep. These include muscle spasms, movement disorders, gastroesophageal reflux, pain from any source, and obstructive sleep apnea (Scher 1998; T. Ward and Mason 2002). Some drugs can disrupt normal sleep patterns, including paradoxical reactions from medications that are normally sedating. Hospitalization and recurrent illness can also interfere with consistent sleep, as normal routines are disrupted (Scher 1998; T. Ward and Mason 2002).

Management

Managing sleep problems starts with an evaluation for sources that can interfere with sleep. A thorough review for sources of discomfort that

can disrupt sleep is essential. Obstructive sleep apnea should be considered when a child is noted to have any of the following: snoring, labored breathing during sleep, and episodes of increased respiratory effort associated with lack of airflow and pauses in snoring, followed by gasping or arousal. When such features are identified, further evaluation can be done with a polysomnogram (sleep study).

When sleep problems are linked to symptoms such as pain or muscle spasms or result from an underlying problem such as obstructive apnea, treating the underlying problem may improve sleep. Pain treatment can improve sleep for two reasons: it treats a source of sleep disruption and it uses medications that are sedating. For some pain medications, such as gabapentin, half of the total daily dose can be given in the evening, with the other half divided into morning and afternoon doses. This schedule is especially helpful when pain behaviors increase in the evening and overnight.

Nonpharmacological interventions include a consistent bedtime and routine, a dark and quiet environment, a comfortable room temperature, and stimulus control (Jan et al. 2008). Medications to consider include melatonin and clonidine (Dodge and Wilson 2001; Jan et al. 2007; Pelayo et al. 2004; Ross, Davies, and Whitehouse 2002; Schnoes et al. 2006; Szabadi 2006). Benzodiazepines tend to be overused, leading to dependency and tolerance. They should be taken only in the short term, then discontinued or tapered.

A number of studies have documented the effectiveness of melatonin in reducing the time it takes to fall asleep for children who have sleep difficulties caused by blindness or any defect of the brain that impairs sleep-wake regulation (Dodge and Wilson 2001; Jan et al. 2007; Pelayo et al. 2004; Ross, Davies, and Whitehouse 2002). In one study, when melatonin was administered in doses ranging from 2.5 to 10 mg before bedtime, approximately three-quarters of the children were able to fall asleep faster (Ross, Davies, and Whitehouse 2002). Melatonin can also improve the ability to stay asleep and the length of sleep for some children. It is most effective when given every night and at the same time each night. When melatonin is used for children who have SNI, some studies have advocated that, as the severity of disability increases, higher doses—occasionally, even up to 15 mg—may be beneficial (Jan and Freeman 2004). No significant adverse events were identified in a study of long-term use of melatonin in children, with a dose of 3 to 6 mg and mean time to follow-up of 3.7 years (Hoebert et al. 2009). In this study, sleep improved in most children, mood improved in many, and discontinuation often led to a relapse of sleep-onset insomnia.

Ramelteon, a medication that stimulates the melatonin receptors in the SCN, is another option, though it has been studied mostly in adults. It was reported to benefit two youths, ages 7 and 18 years, with autism (Stigler, Posey, and McDougle 2006). For both boys, ramelteon was initiated at 4 mg every night, with the dose increased to 8 mg in the 7-year-old. Year-long administration of ramelteon in adults was found to be well tolerated as well as beneficial for sleep (Richardson et al. 2009). The long-term safety of ramelteon for humans is unknown.

Alterations in arousal and wakefulness

As summarized above, wakefulness and sleep are affected by the on-off regulation between the VLPO and branches of the ascending arousal pathway. Just as sleep can be altered, wakefulness can also be altered when the pathways involved in this regulation are impaired.

Lesions along the ascending tracts involved in arousal are thought to contribute to such sleep disorders as narcolepsy and cataplexy. Features can include difficulty in maintaining arousal and the loss of muscle tone. There is limited information about other, similar disorders of the CNS, mostly studied in adults who have such conditions as dementia and Parkinson disease.

Zachary is a 15-year-old boy who has SNI, seizure disorder, and spasticity. He is being assessed for a prolonged episode of being difficult to arouse. His home care nurse is concerned because his tone is "floppy," something that is not normal for Zachary. His history is negative for any contributing causes, with no changes in his medications for many months and no recent illness. His seizure disorder is stable, with no recent seizure. Findings on evaluation also are negative, including a valproic acid level that is unchanged from its usual baseline, normal liver enzymes, and normal (not elevated) ammonia level. It turns out that Zachary has had similar episodes before, when he is difficult to arouse during the day for several hours, then wakes up "suddenly" and is back to his prior baseline. He also has a history of intermittent hypothermia, suggesting impairment in the area of the hypothalamus. Impairment in the pathways involved in arousal and sleep are considered the cause of Zachary's current and past episodes of impaired arousal.

Summary of sleep changes and their management

- Sleep problems are common in children who have SNI, occurring at a higher frequency in those who have midline defects or severe

impairment of the brain (suggested when other alterations in hypothalamic function are present) or those with significant visual impairment.

- Other problems that can interfere with sleep include muscle spasms, obstructive sleep apnea, gastroesophageal reflux, and pain from any source. Identifying and treating a problem that can interfere with sleep will improve sleep.
- It is also important to provide a consistent bedtime and routine, a dark and quiet environment, and a comfortable room temperature.
- Melatonin has an important role in treating sleep problems that may result from a brain defect that interferes with sleep-wake regulation; this includes midline defects that result in altered hypothalamic function. Higher melatonin doses may be beneficial for children who have SNI, up to 10 mg given nightly (there are reports of up to 15 mg, though the effect of long-term use of higher doses is unknown).
- Ramelteon may have a role for older children, though there are limited studies for its use in children.
- Other possible medications include clonidine. Part of its benefit may be its disinhibition of the VLPO, resulting in inhibition of the ascending arousal pathway. Clonidine can also improve other problems seen in many children who have SNI.
- Gabapentin and nortriptyline can be considered when pain appears to be interfering with sleep.
- Benzodiazepines should be used only in the short term, as they become less effective over time and can cause agitation in some people.

CHANGES IN TEMPERATURE AND HEART RATE

For parents, it is unsettling to encounter a significant alteration in their child's temperature or heart rate. An elevated temperature (hyperthermia) will raise concerns about an infection. Changes in the heart rate may result in fears that the child's heart is damaged, that the heart "can't handle" the increased heart rate, or, alternatively, that the child could die from a lowered heart rate. Most parents will be reassured when they learn the reason for the change. And some children will benefit from a care plan that addresses the associated problems.

In general, children who have SNI are at risk for "abnormal" temperature and heart rate as a result of impairment of the hypothalamus and

other areas of the brain that are responsible for regulating the autonomic nervous system and maintaining homeostasis. As an example, impairment of the hypothalamus can alter its ability to regulate temperature, sweating, shivering, and heart rate.

Body temperature

A review of the literature identified the following data on the mean (average) and range of body temperatures for men and women, taken at several body sites (Sund-Levander, Forsberg, and Wahren 2002):

	Mean	Range (2 standard deviations)
Oral	97.7 °F (36.5 °C)	92–100.6 °F (33.2–38.1 °C)
Tympanic (ear)	97.9 °F (36.6 °C)	96–99.5 °F (35.5–37.5 °C)
Rectal	98.6 °F (37 °C)	98–99.5 °F (36.7–37.5 °C)

This information is a helpful guide for a general range of temperatures that might be expected in children, excluding infants younger than 6 months of age. In general, a temperature is considered elevated when it is greater than 100.4 °F. A fever is not, itself, dangerous, but it may indicate an illness from an infection. A temperature is considered potentially dangerous only when it is above 106 to 107 °F (41.1 to 41.7 °C). On the low end, hypothermia is generally defined as a body temperature below 95 °F (35 °C).

Many children who have SNI have changes in the ability of their CNS to regulate body temperature. Both high and low extremes of temperature can be seen, as a result of hypothalamic dysfunction altering the mechanisms of body temperature regulation. Typical temperature-change responses that may be lacking include constriction or dilation of the blood vessels (referred to, respectively, as vasodilation and vasoconstriction), sweating, and shivering. These are responses that help the body adjust when the temperature is too high or too low. In general, other sources are considered before concluding that hypothalamic dysfunction (i.e., impaired central regulation) is the explanation for recurrent hyperthermia or hypothermia.

Elevated body temperature: hyperthermia

One possible cause of hyperthermia is drug toxicity resulting from serotonin syndrome or neuroleptic malignant syndrome. Though these syndromes may be uncommon in children, it is important to be aware of

drugs recently started that could be implicated as a cause. (This topic is covered in more detail in the discussion of medication toxicity in chapter 4 and in the section "Autonomic dysfunction" in chapter 7.) Certainly, fever from an infection is an important consideration.

Once a pattern of elevated temperatures with no infection is established, it is reasonable to consider the child to be at risk for future episodes, due to impaired central control of body temperature. With future episodes, medical providers can help parents feel comfortable taking a watchful approach and avoiding unnecessary repeat testing, while observing the child for clues that suggest an infection as the source of fever. Information to empower parents and assist with this process can come from asking the following questions:

- If you did not know that your child's temperature was elevated, would you be worried about how your child is doing?
- Does your child look sick or look more like his or her usual self?
- Are there other symptoms to suggest an infection?
- How does your child usually look when he or she is sick with a specific illness and infection?
- How does your child look when his or her temperature is elevated without a specific cause?
- What other features are identified at such times? Does your child have other features to suggest an autonomic storm, such as facial flushing, sweating, tachycardia, retching, agitation, arching, or stiffening?
- How does your child respond to interventions to bring down the temperature?

Exposure to an elevated environmental temperature is another possible cause of hyperthermia, given diminished normal regulatory responses such as sweating and vasodilation (MacKenzie et al. 1991; MacKenzie et al. 1995). Interventions that help decrease body temperature include a fan, cool wet towels, and repositioning. If there are associated symptoms that suggest an autonomic storm, medications may offer benefit, such as intermittent use of clonidine, morphine sulfate, or a benzodiazepine.

Low body temperature: hypothermia

Children who have SNI are at risk for recurrent hypothermia due to hypothalamic dysfunction. Hypothyroidism can also lower the body's

temperature, though typically the temperature does not fall as low as it does with hypothalamic dysfunction. Children with hypothermia should have their typical temperature range documented; parents and others need to be aware that a temperature above this artificially low range may be indicating a fever, even if that temperature is not normally considered a fever.

In general, children who have SNI and a temperature lower than 95 °F may have no other concerning features. Some parents have noted no concerns, but have then observed an increase in alertness once the temperature rose above 94 or 95 °F. Some complications associated with hypothermia are acute pancreatitis and lowered blood cell counts, including anemia and thrombocytopenia (low platelet count) (Collins and Danzl 2006; Metz et al. 1996). In one case series of children with SNI and acute pancreatitis, central hypothermia was identified as the likely source when no other cause was found (Hauer 2008). These complications occur infrequently as a result of hypothermia, and they probably require significant hypothermia for a prolonged period, such as a body temperature less than 92 °F for longer than 6 to 8 hours.

To avoid these unwanted effects, the goal is to keep a child's temperature above 94 to 95 °F. Interventions include the use of a hat and scarf to minimize heat loss through the head and neck, as well as gloves, thick socks, and blankets. Children need these measures because their bodies cannot regulate heat loss normally through shivering and vasoconstriction in the skin (which minimizes heat loss) in response to a low temperature (MacKenzie et al. 1991; MacKenzie et al. 1996). Cyproheptadine may offer benefit for some children, based on a few case reports (Kloos 1995; Ruiz et al. 2003; Sheth, Barron, and Hartlage 1994).

Individuals who have SNI and hypothermia are also at risk for excess caloric intake and weight gain, as a result of decreased oxygen consumption and energy expenditure (Dickerson et al. 2003; MacKenzie et al. 1991). This is covered in greater detail in the section "Growth and nutrition" later in the chapter.

Heart rate

It can be frightening for parents to observe a heart rate of 40 in their sleeping child or to see their child's heart rate intermittently reaching 170. Children who have SNI are at risk for such changes from the expected average range of heart rate for the child's age. As a guideline, average heart rates by age are approximately as follows:

Age (years)	Heart rate (beats per minute)
<1	110–160
1–5	100–150
5–10	80–120
>10	60–100

Fast heart rate: tachycardia

Illness, fever, and dehydration are common causes of an elevated heart rate, or tachycardia. Children who have SNI are also at risk for an intermittently elevated heart rate as a result of pain, medication toxicity or withdrawal, and autonomic dysfunction. The child's medical history will reveal whether any medication was recently started or stopped and, if so, whether there are other features that may suggest drug toxicity or withdrawal. As reviewed in greater detail in chapter 7, autonomic dysfunction should be considered when tachycardia occurs with other associated features, including flushing and redness of the face, sweating, retching, agitation, arching, and stiffening. Chapter 4 describes pain as a contributing factor.

The heart rate of some children who have SNI may reach 130 to 150 beats per minute and may be higher at times of pain and illness. For a child with a normal heart, tachycardia is not harmful to the heart. An ECG can assess the heart's conduction system. When tachycardia occurs, the goal is to identify and treat contributing problems such as pain and autonomic dysfunction. When the child is more comfortable, the upper range of the heart rate will not be as high.

Slow heart rate: bradycardia

Children who have SNI are also at risk for a low heart rate, or bradycardia, as a result of low metabolic rate, hypothyroidism, medications, and autonomic dysfunction. Rarely, bradycardia can result from a defect in the electrical conduction system in the heart. This can be identified with an ECG. Children with bradycardia can be evaluated for hypothyroidism with a blood test. Medications that can contribute to slowing of the heart rate include clonidine and beta-adrenergic antagonists (beta blockers) such as propranolol, which is sometimes used to treat the hypertension and tachycardia associated with autonomic dysfunction. Autonomic dysfunction should be suspected when there is no other explanation; hypothermia

and slow intestinal motility are other symptoms of autonomic dysfunction. The heart rate can become even lower when the child is sleeping, often falling to the high 30s or low 40s.

Parents can be reassured about these numbers, which can be a source of great distress. It is not uncommon to notice no other changes in the child. In fact, one likely reason that such low heart rates can be tolerated in children who have SNI is the low energy expenditure as a result of their limited activity. A heart rate that is gradually slowing over time may reflect a more global change in the CNS. For these children, it may be helpful to minimize the effect of other contributing factors, such as maintaining a body temperature above 94 to 95 °F (35 °C) with the use of hats, gloves, and blankets.

When there is no other explanation for a low heart rate that gradually declines, with other changes, it may be an indication of irreversible deterioration in critical areas of function in the brain. Other features may include increased sleeping, intermittent pauses in breathing (apnea), decreased body temperature, cool hands and feet that are mottled or blue, and slowing of intestinal function that may be noted as increasing feeding intolerance. Such changes are often intermittent and transient initially, occurring over months. These changes are covered in detail in chapters 7 and 10.

ENDOCRINE ISSUES

The hypothalamus, as noted earlier, is involved in linking the endocrine system with the nervous system. For example, hormones from the hypothalamus stimulate the release of hormones from the pituitary gland. In this section I review some of the problems created by alterations in the endocrine regulation of the hypothalamus and pituitary gland in children with SNI, including early-onset puberty, osteoporosis (low bone density), changes in water and sodium regulation, thyroid hormone deficiency, and growth hormone deficiency. Other, associated issues are also covered, including management options for menstrual bleeding and growth attenuation.

Early puberty

Puberty is generally considered to be early if pubertal changes occur before 8 years of age in girls and 9 years of age in boys; this is also referred to as precocious puberty. Menarche (menstruation or menstrual period) is

considered premature if it occurs before 10 years of age. A child's race/ethnicity can influence the timing of puberty; earlier pubertal development has been reported in African American and Hispanic/Latina girls (Rosenfield, Lipton, and Drum 2009). A high BMI has also been associated with earlier pubertal development in girls (Rosenfield, Lipton, and Drum 2009). A cross-sectional survey of children with moderate to severe cerebral palsy found that girls entered puberty earlier but tended to complete puberty later than did boys with CP (Worley et al. 2002).

Isolated features of puberty occurring early can often be benign. When caused by an underlying medical condition, early puberty is divided into central and peripheral precocious puberty. Concerns about precocious puberty include both the possible underlying cause and the early end it brings about in linear growth, resulting in the child being shorter than he or she would have been with later puberty.

Benign early development of pubertal features includes premature thelarche and premature adrenarche. Premature thelarche is a benign, idiopathic condition manifested by isolated breast development before puberty. Most girls with premature thelarche do not progress to precocious puberty. Premature adrenarche is the early secretion of adrenal androgens, resulting in the premature appearance of pubic hair (pubarche), sometimes accompanied by body odor, acne, and underarm hair. Neither condition requires medical treatment.

Children who have SNI are at risk for central precocious puberty due to early activation from the hypothalamus. Many insults to the CNS can cause central precocious puberty, including traumatic brain injury, lack of oxygen to the brain, malformations of the brain, and genetic disorders. One retrospective review of early puberty in children with a developmental disability estimated that these children are at least 20 times more likely to experience early pubertal changes than typically developing children (Siddiqi et al. 1999). In this study, the average age at onset of pubertal changes was 5 years 11 months for girls and 7 years 2 months for boys. Of the 27 girls in the study, 14 were classified as having central precocious puberty; 6, premature adrenarche; 4, premature thelarche; and 3, idiopathic precocious puberty. Only 5 boys were identified as having precocious puberty. In the same study, the option of treatment to stop further sexual development and optimize adult height was declined by some parents, with the view that improving their child's height was not a priority for their profoundly disabled child.

Early puberty in children who have SNI raises two questions: how much testing to consider and whether treatment should be used to delay further

pubertal development. Tests include (1) obtaining a bone age (by X-ray, typically of the wrist); (2) blood tests, including follicle-stimulating hormone (FSH), luteinizing hormone (LH), and dehydroepiandrosterone sulfate levels, gonadotropin-releasing hormone (GnRH) stimulation test, testosterone level (in boys), and estradiol level (in girls); (3) MRI/CT of the head; and (4) pelvic ultrasound. Not every child needs every test. The sex of the child is factored into the degree of testing to consider; girls who have SNI are much more likely than boys to have early pubertal development, and this development is more likely to be a benign result of the underlying CNS impairment.

Children with isolated breast development or pubic hair growth typically do not need testing or treatment. Treatment for precocious puberty uses a GnRH agonist, such as leuprolide acetate (Lupron). This medication supplies a negative feedback, resulting in decreased levels of LH and FSH 2 to 4 weeks after initiating treatment. For children who have SNI, it may be more beneficial not to use treatment, thus limiting the child's final height, which can make it easier to lift, transfer, and transport the child. This is given further consideration later in the chapter ("Growth attenuation").

As always, clinical decisions should be based on what the family believes to be in the best interest of their child. Parents should not see decisions to limit testing or treatment as treating their child differently because of his or her disability. Healthcare providers who have a long-term relationship with the family can play a crucial role in translating information, reviewing the risk of a test, such as the sedation required for head imaging, and making sure that parents' fears are identified and addressed.

Menstruation and hygiene

Medical interventions

Pubertal changes in girls bring concerns from parents and caregivers about hygiene and questions about options for menstrual suppression (Dizon, Allen, and Ornstein 2005). Medical options include the injectable progesterone depot medroxyprogesterone acetate (Depo-Provera), oral contraceptives, and the transdermal contraceptive patch. The goal of these medications is to diminish or eliminate menstrual bleeding. In a retrospective review, almost 60% of the parents of premenarchal girls with developmental disabilities opted to take a "wait and see" approach after they had received information about medical options for menstrual suppression (Dizon, Allen, and Ornstein 2005). Of the wait-and-see group, 22% later returned to initiate an intervention. This study suggests the benefit of anticipating such

concerns and providing information to families before their daughter begins menstruating.

In this same retrospective review, Depo-Provera was the most commonly prescribed and accepted method of menstrual suppression for women with developmental disability (Dizon, Allen, and Ornstein 2005). Depo-Provera must be considered cautiously, however, because it carries the risk of decreasing bone mineral density (BMD) over time (ACOG 2009; Dizon, Allen, and Ornstein 2005; Savasi et al. 2009). This is an important consideration for nonambulatory children who have SNI, especially given the other risk factors for low BMD, as covered in more detail below ("Osteoporosis").

Continuous oral monophasic (same dose every day) low-dose estrogen-progestin can be used to achieve amenorrhea (no menstrual period), by taking the "active" tablets but skipping the placebo pills (ACOG 2009; Backeljauw, Rose, and Lawson 2004; Savasi et al. 2009). This medication regimen may also decrease other symptoms that accompany menstruation, such as cramping or behavioral changes, by eliminating the hormonal fluctuation that can cause these symptoms. Caregivers should be told that the occurrence of bleeding with continuous use of an oral contraceptive is greatest in the third month, then decreases, with one study reporting 81% of patients achieving amenorrhea by week 24 (Machado et al. 2004). This method can result in unplanned breakthrough bleeding, so a 7-day pill-free period every 4 to 6 months can be used, if necessary, to prevent spotting. Some girls and women may need to transition through a pattern of withdrawal bleeding every 7 to 10 weeks to achieve amenorrhea. One study suggests that, of the oral contraceptives, norethindrone acetate resulted in more amenorrhea than levonorgestrel (ACOG 2009). Weekly patches containing ethinyl estradiol combined with a progestin can also be used continuously; patches are replaced weekly for 9 weeks, followed by a 7-day patch-free period to achieve withdrawal bleeding.

One risk with oral contraceptives is a very low yet increased risk of deep vein thrombosis (DVT; a blood clot, typically in a leg vein), of particular concern for nonambulatory individuals. In a large cohort study of girls and women aged 15 to 49, the overall absolute risk of DVT per 10,000 woman-years in nonusers of oral contraceptives was 3.01 and in current users was 6.29 (Lidegaard et al. 2009).

For nonambulatory individuals, the concern should be kept in perspective, as thrombosis in children and young adults with CP is very rare and, if it occurs, may do so only with other risk factors. In a retrospective review of 57 severely disabled residents in a long-term care facility, no cases of DVT or pulmonary embolism were identified, even though 60% of the

residents had an additional risk factor (Rousseau and Guillotel 2001). The mean age was 28 years and mean duration in the institution was 18 years. For the patients with at least one additional risk factor, these factors included orthopedic surgery, bone fractures, and hormonal treatment. The speculation is that there may be a protective benefit of spasticity, with improved circulation with daily movement and weekly physical therapy, even though the individual is otherwise not mobile.

There is one case report of a DVT in a 36-year-old nonambulatory woman with SNI who was taking an oral contraceptive (Lohiya et al. 2005). Eight months prior to the DVT, the woman's oral contraceptive had been changed from one with 35 μg of ethinyl estradiol to one with 50 μg of mestranol, resulting in a higher estrogen dose (Lohiya et al. 2005).

The risk of a DVT is lower when the estrogen dose is less than 40 μg. The progesterones levonorgestrel and norethindrone have a lower risk of DVT than the third-generation progesterones desogestrel and gestodene (Lidegaard et al. 2009; van Hylckama Vlieg et al. 2009). The risk decreases with the duration of use after the first 1 to 2 years. The risk of thrombosis caused by oral contraceptives is also greater for women who are obese and women older than 30 years. Two studies comparing oral contraceptives with the transdermal contraceptive patch found mixed results: one identified the same risk and the other found a higher risk with the patch (Cole et al. 2007; Jick et al. 2007). Temporary discontinuation of an oral contraceptive may be considered before surgery, because of the added risk of DVT during the postoperative period, especially if there is an added risk factor such as being older than 30 years. The family history should be reviewed for occurrences of DVT or pulmonary embolism that may indicate an inherited risk of a blood clotting disorder.

When evaluating someone for a possible DVT, measurement of plasma D-dimer (a fibrinolysis product) is a useful test. A negative result virtually rules out a DVT. An elevated D-dimer is very sensitive for DVT and pulmonary embolism (a test that is very *sensitive* is one that is likely to be positive when the problem is present, but can also be positive when the problem is not present—referred to as a false positive) but is less specific (a test that is less *specific* can have a negative result even though the problem is present—referred to as a false negative). An elevated D-dimer requires a diagnostic study with a venous Doppler ultrasound to determine whether the elevated level is correct or is a false positive.

Some medications can alter the metabolism of oral contraceptives. Medications that are enzyme inducers, such as certain antiepileptic drugs (AEDs, including phenobarbital, phenytoin, carbamazepine, oxcarbaze-

pine), decrease the effectiveness of an oral contraceptive through increased metabolism.

To summarize the information on oral contraceptive use and BMD and DVT:

- Depo-Provera, an injectable progesterone, increases the risk of low BMD (osteoporosis) and bone fractures, a significant factor in nonambulatory children who have SNI (see "Osteoporosis" below).
- Oral contraceptives can increase the risk of DVT.
- These two risks can be weighed by considering the individual's risk of low BMD (risk factors include lack of weight bearing and certain antiepileptic drugs) versus the risk of a DVT. Is there a family history to suggest an increased risk of DVT? Is the person older than 30 years, an age at which risk increases?
- Nonambulatory children with neurological impairment seem not to be at significant risk for DVT.
- The risk of DVT with a combination oral contraceptive can be lowered by selecting one with the progesterone levonorgestrel or norethindrone rather than one with desogestrel or gestodene.
- The risk of DVT is also lower in a combination oral contraceptive with an estrogen dose of less than 40 μg.
- Femcon Fe is a chewable form that can be dissolved in water and given by G tube. It contains 35 μg of ethinyl estradiol and norethindrone. Other oral contraceptives can be considered.
- To achieve amenorrhea, the "active" oral contraceptive tablets can be taken daily, while skipping the placebo pills. This regimen may also lessen other, associated symptoms such as cramping or behavioral changes by eliminating hormonal fluctuation.
- The occurrence of bleeding with continuous use of an oral contraceptive is greatest in the third month, then decreases.
- A 7-day pill-free period every 4 to 6 months can be used, if necessary, to prevent spotting. As an example, an extended cycle of combined oral contraceptive with 30 μg of ethinyl estradiol and levonorgestrel was developed, to be taken for 84 days followed by 7 days of a placebo.
- It is unclear whether the DVT risk is the same or higher with the transdermal contraceptive patch rather than an oral contraceptive.
- Obesity and age greater than 30 years increase the risk of DVT while taking an oral contraceptive.

- A family history of abnormal blood clotting, such as DVT, especially at a young age (younger than 50 years), suggests the possibility of an inheritable clotting disorder.

Hysterectomy

Surgical interventions to manage abnormally heavy bleeding include endometrial ablation and hysterectomy. Endometrial ablation is not recommended for children who have SNI, when the goal is to eliminate menstrual periods for the benefit of hygiene. The incidence of amenorrhea in adults following this procedure ranges from 13% to 47%, a smaller incidence than with oral contraceptives (ACOG 2009).

Before considering a hysterectomy, it is necessary to know the state law regarding court approval for such a procedure in a person unable to give consent. The most common reasons for considering hysterectomy include elimination of menstrual bleeding and prevention of pregnancy. The latter risk is much more significant in adolescents with mild to moderate intellectual impairment and normal motor function, because this group is more independent and therefore more vulnerable to unsupervised contact, increasing the risk of sexual contact without consent. The American Academy of Pediatrics (AAP) and the American College of Obstetrics and Gynecology (ACOG) recommend that medical interventions be utilized first and that hysterectomy should not be the initial treatment for dealing with menstruation in individuals who have disabilities (AAP 1999; ACOG 2007).

Ashley treatment

Ashley treatment is a set of medical and surgical procedures that were used for a child, "Ashley X," who had SNI—a case that was considered controversial. The interventions included growth attenuation with high-dose estrogen, hysterectomy, bilateral breast bud removal, and appendectomy. The information presented here is intended to help when considering these interventions for children who have SNI.

I should note, first of all, how Ashley's parents benefited the medical community by bringing attention to the worries and goals of parents and the need for careful consideration of the interventions that might best address these worries and goals. Unfortunately, one of the greatest harms generated by the original report that described Ashley treatment was its lumping all of the interventions, including the decision to perform a hys-

terectomy, under the label "growth attenuation" (Gunther and Diekema 2006). As noted above, hysterectomy is not recommended without first pursuing other approaches to care. In addition, there is an assumption of a benefit to be gained from growth attenuation that is not at all certain (Feudtner 2011).

This case generated a significant amount of debate and concern. Of interest here is that other surgical interventions are used for individuals with SNI with only limited evidence to drive the decision, without generating controversy. What probably adds to the controversy and challenge of weighing the risks and benefits of such options as growth attenuation is that these options do not fit within the traditional medical model of benefit versus harm to health. Instead, the interventions focus on how much a child's life might improve when the care that can be provided is improved. Unfortunately, goals are being used to defend interventions. Goals are best met when they are well defined, with the various methods for meeting these goals explored equally, especially when an intervention has unclear long-term benefit and risk.

To best address the options considered and ultimately implemented for Ashley, it is helpful to break them down into the several components that were part of Ashley's treatment:

- Decreasing body size by decreasing the final length/height of a child who remains dependent on others for all physical care
- Decreasing size by minimizing excessive weight gain
- Eliminating breast development
- Addressing hygiene and discomfort associated with menstrual periods
- Eliminating the risk of breast and uterine cancer
- Eliminating the risk of pregnancy resulting from sexual assault

I will not attempt to summarize all of the ethical considerations, which have been covered in great detail elsewhere (Kirschner, Brashler, and Savage 2007; Wilfond et al. 2010), but try to provide a full consideration of each separate area of concern, and the options available for addressing these concerns (table 8.1). Some information is covered in greater detail elsewhere in the chapter. When considering such interventions, it is important to recognize the differences between women and girls who have intellectual impairment and normal motor ability and those who have SNI.

TABLE 8.1 Components of Ashley treatment

Target of treatment	Comments
Final length/height (growth attenuation)	• Benefit and long-term risk unclear • High-dose estrogen expected to diminish the final height of a child who has SNI • Using data from normally developing girls treated with high-dose estrogen for growth attenuation, estimated that the reduction would be >6 cm (2.36 inches) • A greater reduction depends on earlier initiation, such as at onset of pubertal changes and before menses • The short-term risk of high-dose estrogen may be similar to the risk of combination oral contraceptives over a longer period of time • High-dose estrogen can theoretically be used in boys, though no information on the safety of estrogen administration in males • See text discussion "Growth attenuation"
Final weight	• Children who have SNI are at risk for excessive weight gain, especially those with hypothermia, limited movement of extremities, and interventions that decrease tone, such as intrathecal baclofen pump • Earlier attention to minimizing weight gain (total energy intake) that is balanced with sufficient nutrition (protein and micronutrients) may also decrease the final height • Not emphasized in Ashley treatment • When tube feedings need to be restricted, micronutrients and protein can be supplemented • See text discussion "Growth and nutrition"
Breast development	• Breast size in girls who have SNI may partly reflect excess weight gain, though no information on this issue • The extent to which breast development affects comfort and care is unknown
Menstrual periods: hygiene and comfort	• Medical interventions such as oral contraceptives are recommended before consideration of hysterectomy • Use of hysterectomy in a disabled individual unable to provide consent may require court approval • See text discussion "Menstruation and hygiene"
Risk of breast and uterine cancer	• Breast bud removal and hysterectomy not routinely done for these reasons
Risk of sexual assault and pregnancy	• Hysterectomy and breast bud removal do not remove the risk of sexual assault; efforts need to be maintained to eliminate this risk for all vulnerable children and adults

TABLE 8.1 *(continued)*

Target of treatment	Comments
	• The risk for women and girls who have SNI is probably lower than that in the general population, and especially compared with that for young women with intellectual disabilities and normal motor function, at risk due to impaired judgment and impulsive behaviors

Growth attenuation

Growth attenuation (reduction) with high-dose estrogen was first used in normally developing girls thought to be becoming "undesirably" tall. From that experience came the recognition that this treatment could be applied to girls who have SNI, to achieve the goal of smaller size for someone who would remain dependent on others for care (Gunther and Diekema 2006). The approach is similar to a family choosing not to treat precocious puberty, in order to minimize a girl's final height. The normal body levels of estrogen during the pubertal growth spurt accelerate growth, but estrogen doses above these levels can inhibit growth. This results from a rapid maturation of the growth areas in the long bones of the legs and arms (the epiphyseal growth plates), resulting in an earlier stop to linear growth.

Using data from normally developing girls treated with high-dose estrogen for growth reduction, it is estimated that the reduction in final height would be more than 6 cm, or 2.36 inches (Allen et al. 2009). The final height depends on when the high-dose estrogen is initiated, with a greater reduction in height when initiated earlier, such as at the onset of pubertal changes and before menses. Just as with combination oral contraceptives, high-dose estrogen can increase the risk of DVT. A review of other risk factors, as already outlined in the discussion of oral contraceptives, can guide the risk and benefit of this intervention. High-dose estrogen can, theoretically, be used in boys, though there is no information on the safety of estrogen administration in males. A pediatric endocrinologist must be involved when high-dose estrogen is being considered for growth attenuation. The endocrinologist will prescribe dosing, timing, and follow-up. The intended benefit and long-term risk remain unclear.

Osteoporosis: low bone mineral density

Children who have SNI are at risk for osteoporosis, a bone mineral density that is significantly below the expected level for the average, healthy individual (Henderson et al. 2005; Henderson, Lark, Gurka, et al. 2002). Low BMD increases the risk of developing a fracture, as was found in children with moderate to severe CP (Henderson, Lark, Gurka, et al. 2002).

Lack of weight bearing is one of the greatest risk factors for osteoporosis in children who have SNI. Other factors include calcium and vitamin D deficiency, lack of sun exposure, anticonvulsant therapy (phenytoin, phenobarbital, carbamazepine, valproic acid), and a history of prematurity (Mascarenhas, Meyers, and Konek 2008). Unlike in elderly adults, in children who have SNI, osteoporosis is not primarily a result of true losses in bone mineral but rather a diminished rate of growth in bone mineral compared with the rate in healthy children (Henderson et al. 2005).

As would be expected, the risk factors for a fracture are the same as those for development of osteoporosis, including lack of weight bearing and use of AEDs. In a retrospective study of patients with CP who received treatment for a fracture (156 patients, 238 fractures), the mean age for the first fracture was 10 years (range 1 to 21 years), with 82% of fractures occurring in a lower extremity (Presedo, Dabney, and Miller 2007). The cause of injury was unknown for 55% of the fractures. The diagnosis was considered delayed in 46% of cases, with pain evolving over several days as the most typical symptom. Approximately 25% of the patients had multiple fractures, with these accounting for half of all fractures. The patients with multiple fractures had a significantly higher use of AEDs than those with a single fracture.

In a study of predictors of low BMD, the weight *z* score (standard deviation, which is the variation from the average) proved to be the best predictor of the BMD *z* score (Henderson et al. 2004). Declining BMD *z* scores also correlated with increasing age and greater severity of impairment. As an example, a 10-year-old nonambulatory child who had quadriplegic CP and a "typical" weight *z* score of –2 would be predicted to have a BMD *z* score that is, at best, –2. Other risk factors identified include prior fractures and use of anticonvulsants associated with low BMD.

Improved nutrition in children who had CP resulted in a significant increase in bone mineral content (BMC), as measured by dual emission X-ray absorptiometry (DXA or DEXA), though this did not translate to an in-

crease in the BMC standard deviation score (*z* score) between baseline and repeat testing (Arrowsmith et al. 2010). Significant increases in body fat and protein were also identified in these children, with a greater increase in body fat.

Assessment of bone mineral density

There are limitations with a DXA scan in the assessment of bone mineral density in children who have SNI. Problems that can interfere with the interpretation of measured BMD include surgically placed hardware, abnormally shaped bones, previous fractures, and difficulty in proper positioning of the patient for scanning the bone region of interest (hip, spine, arm, and distal femur). Muscle contractures in the hips and arms, or scoliosis in the spine, can impede the ability to replicate the same position from scan to scan. If the patient's position changes from one scan to the next, the test results will indicate a false bone density change.

Vitamin D intake and supplementation

Minimizing the risk of osteoporosis includes identifying and providing an adequate intake of calcium, phosphorus, and vitamin D. Certain AEDs are associated with lowering of the vitamin D level in the blood. These drugs include carbamazepine, phenobarbital, phenytoin, and valproic acid. If a child is taking an antiepileptic drug associated with low BMD, supplementation with vitamin D may improve bone density (Gissel, Poulsen, and Vestergaard 2007; Jekovec-Vrhovsek, Kocijancic, and Prezelj 2000).

The goal is to maintain a blood level of 25-hydroxyvitamin D, or 25(OH)D, of more than 30 ng/mL (75 nmol/L). A level below 20 ng/mL (50 nmol/L) is considered a deficiency. To convert a measured 25(OH)D level to the international unit of nmol/L, the ng/mL level is multiplied by 2.496.

Recommended vitamin D intake depends on the 25(OH)D level and on whether a child is taking an AED that increases the risk of osteoporosis. General guidelines include the following (Drezner 2004; Holick 2007):

- The recommended daily vitamin D_3 (cholecalciferol) intake is 800 to 2,000 IU (international units).
- The higher dose of 2,000 IU is appropriate for children taking multiple AEDs or with limited sun exposure.
- Treatment options for a 25(OH)D level of less than 30 ng/mL (75 nmol/L) include ergocalciferol (vitamin D_2), 50,000 IU, one

day per week for 8 weeks, given as 6.25 mL of liquid ergocalciferol (8,000 IU/mL).

Calcium supplementation

Calcium supplementation is based on recommendations for children by age (Greer and Krebs 2006). For children 4 to 8 years of age, the recommendation is 800 mg (20 mmol) of calcium per day; for children 9 to 18 years of age, 1,300 mg (32.5 mmol) per day. Excessive calcium intake can increase the risk of kidney stones and should be avoided.

Weight bearing in a stander

Providing weight bearing with a stander seems to improve bone mineral density in nonambulatory children. A study of 18 children with CP, both nonambulatory and ambulatory, found an increase in femoral neck BMD (Chad et al. 1999). The study compared a program of weight bearing and physical activity with no intervention in the control group. In a randomized trial including 26 prepubertal nonambulatory children with CP, the intervention group, with a 50% increase in time spent standing over a 9-month period, was compared with a group with no change, with a range of 180 to 675 minutes of standing per week (Caulton et al. 2004). There was a 6% increase in spinal BMD in the intervention group compared with the control group, with no change noted in tibial BMD.

Physical therapists and orthopedic specialists can identify the stander equipment that is best suited for each child and provide a suggested standing schedule. For children with poor head control, the supine stander is a good option. The scheduled time in the stander is often gradually increased, from 10 to 15 minutes initially up to an hour twice a day. A parent can factor in how well the child tolerates a recommended schedule.

Vibration

The impact of vibration on bone mineral density has been investigated, though most studies have been in the elderly, including postmenopausal women (Totosy de Zepetnek, Giangregorio, and Craven 2009). In a randomized study of 20 children with CP, whole-body vibration did not result in an increase in BMD measured at the lumbar spine and femoral head (Ruck, Chabot, and Rauch 2010). Whole-body vibration for nonambulatory

children who have SNI and low BMD requires further study to determine whether it has a role in improving BMD in these children.

Bisphosphonate medications

Bisphosphonate medications, such as pamidronate, have been evaluated in children with spastic quadriplegic cerebral palsy and low BMD. These drugs were found to be well tolerated, to increase BMD, and to decrease the fracture risk in the short term (Bachrach et al. 2010; Henderson, Lark, Kecskemethy, et al. 2002). Unfortunately, this benefit for BMD may be lost once treatment is stopped (Bachrach et al. 2006). In addition, the long-term effects on bone remodeling in children are unknown. This is important in the light of the reported risk of subtrochanteric or diaphyseal femur fracture in adults taking bisphosphonates for more than 5 years, though this risk remains unclear (Black et al. 2010).

A recent Cochrane review of bisphosphonate therapy for children with secondary osteoporosis indicated that short-term (3 years or less) bisphosphonate use appears to be well tolerated, though the evidence does not support bisphosphonates as standard therapy (L. Ward et al. 2007). Bisphosphonate use is ultimately guided by the child's risk for future fractures, especially children who have already had fractures.

Summary of osteoporosis and its management

- Low bone mineral density is a common problem in nonambulatory children who have SNI. As a result, bone fractures occur at an increased rate in such children.
- In addition to lack of weight bearing, other factors that increase the risk of low BMD and fractures include inadequate vitamin and mineral intake, lack of sun exposure, and use of antiepileptic drugs that are associated with lowering of the vitamin D level, including carbamazepine, phenobarbital, phenytoin, and valproate.
- Interventions to minimize the development of low BMD include sufficient intake of calcium, phosphorus, and vitamin D, with increased supplementation of vitamin D for children taking AEDs associated with low BMD.
- Vitamin D levels should be monitored annually.
- Calcium supplementation is based on recommendations for children by age.

- Weight-bearing schedules with appropriate stander equipment may minimize low BMD. A suitable schedule and equipment can be reviewed with a physical therapist and orthopedic specialist.
- Bisphosphonate medications, such as pamidronate, may decrease the future risk of a fracture for a child who has SNI and a prior fracture. Bisphosphonates are not recommended as routine treatment for non-weight-bearing children with a low BMD, because their long-term effect is unknown, including potential risk when used for more than 5 years and a decrease in BMD to prior levels once stopped. Bisphosphonate use may be best reserved for children with two or more fractures, with a treatment course limited to 3 years.
- Routine DXA scan screening is of limited benefit, given that bisphosphonate medications are not recommended for routine use. In addition, there are challenges in obtaining accurate information from scans of children with SNI.
- Though not studied, minimizing injury risk is possibly the most important step in the prevention of fractures. Parents can meet with therapists for training in proper transfer techniques and review equipment options to assist with transfers in the home.

Serum sodium regulation

The body regulates water and sodium (Na+) balance, with a measured serum sodium level normally ranging from 135 to 145 mEq/L (milliequivalents per liter). A sodium level below 135 mEq/L is referred to as hyponatremia, and a level above 145 mEq/L is referred to as hypernatremia. I will not attempt to review all causes of an abnormal sodium level. Instead, the focus here is on the problems for which children who have SNI are at greater risk.

Low sodium: hyponatremia

Hyponatremia is usually asymptomatic when serum sodium levels are between 125 and 135 mEq/L. Symptoms and complications are usually seen when the level is less than 120 mEq/L. The severity of symptoms also depends on how rapidly the sodium level decreases. Symptoms can include vomiting, lethargy, restlessness and irritability, muscle spasms, and seizures. Neurological symptoms most often arise with very low serum sodium levels, typically less than 115 mEq/L.

Hyponatremia occurs when an imbalance between the intake and excretion of water results in excess water in the body relative to sodium levels. Water excretion from the kidneys can be inhibited by the inappropriate persistent release of antidiuretic hormone from the hypothalamus. Hyponatremia can also occur if too much sodium is excreted from the kidneys into the urine. Sodium depletion from the kidneys can be caused by a deficiency of aldosterone (mineralocorticoid) due to adrenal gland insufficiency and by the use of thiazide diuretics such as chlorothiazide (Diuril). Damage to the CNS can also result in an inappropriate excretion of sodium into the kidneys, referred to as cerebral salt wasting. Finally, sodium intake may be too low if formula feedings are decreased—for example, to prevent excessive weight gain.

CAUSES

The focus here is on the most common conditions seen in children who have SNI that can result in hyponatremia. Causes to consider include the syndrome of inappropriate antidiuretic hormone, glucocorticoid deficiency, hypothyroidism, and cerebral salt wasting.

The syndrome of inappropriate antidiuretic hormone (SIADH) results from an inappropriate, persistent release of antidiuretic hormone, which decreases the excretion of water. Causes of SIADH include medications, acute injury to the CNS (hydrocephalus, infection, traumatic brain injury), and acute pulmonary infection (Moritz and Ayus 2002). Medications that can cause SIADH include carbamazepine, oxcarbazepine, and selective serotonin reuptake inhibitors (SSRIs). In a study of individuals with intellectual disability who were taking carbamazepine, the mean sodium level was 135.7 mEq/L, with a range of 124 to 144 mEq/L. The control group, not taking carbamazepine, had a mean sodium level of 139.4 mEq/L, with a range of 129 to 154 mEq/L (Kelly and Hillery 2001). Risk factors for hyponatremia while taking carbamazepine can include being older than 40 years and taking other medications associated with hyponatremia (Kuz and Manssourian 2005). Oxcarbazepine resulted in hyponatremia more frequently than did carbamazepine, with a much greater risk for people older than 40 years (Dong et al. 2005). In a study of children taking oxcarbazepine, asymptomatic hyponatremia occurred in 27% (n = 20), and only one child (1.3%) developed clinically significant hyponatremia (Holtmann et al. 2002). The authors concluded that electrolytes should be checked before starting oxcarbazepine and whenever clinically relevant side effects occur.

Hyponatremia caused by an SSRI (e.g., citalopram, fluoxetine, paroxetine, sertraline) is more likely to occur in elderly people and when other

risk factors for hyponatremia exist (Jacob and Spinler 2006). The risk of hyponatremia with the use of SSRIs for children is not clear.

Children who have SNI that includes hypothalamic or pituitary dysfunction can develop glucocorticoid deficiency, either from lack of corticotropin-releasing hormone secretion by the hypothalamus or from lack of adrenocorticotropic hormone (ACTH) secretion by the anterior pituitary. Both hormones stimulate corticosteroid release from the adrenal gland. Hyponatremia as a result of glucocorticoid deficiency is predominantly a result of SIADH, because cortisol is an inhibitor of ADH secretion, such as at times of stress, when cortisol release would normally increase (Liamis, Milionis, and Elisaf 2011). An early morning (8 a.m.) cortisol measurement is a screening test for both causes of glucocorticoid deficiency. A level of less than 3 μg/dL (80 nmol/L) is strongly suggestive; a level greater than 10 μg/dL (275 nmol/L) makes the diagnosis unlikely. Further testing with a cosyntropin (ACTH) stimulation test is needed to confirm the diagnosis. Treatment involves daily replacement with hydrocortisone (cortisol), with an increase in the dose at times of physical stress, such as during an acute illness with fever.

Hypothyroidism can also occur in children who have SNI, as a result of hypothalamic or pituitary dysfunction, and one of its associated problems is hyponatremia, though it is usually mild. Tests for hypothyroidism include measurement of free T4 (thyroxine) and TSH (thyroid-stimulating hormone) levels.

Cerebral salt wasting (CSW) resulting in an excessive excretion of sodium into the kidneys has been described almost exclusively in the acute setting, such as following traumatic brain injury, infection of the CNS (such as from tuberculous meningitis), or removal of a tumor involving the hypothalamus (Huang et al. 2004; Palmer 2003; Taplin et al. 2006). It can be challenging to distinguish CSW from SIADH in these acute settings. One case report identified CSW developing in a child with a congenital structural malformation of the brain (Ozdemir et al. 2010). Experience indicates that CSW may contribute to hyponatremia more chronically in children who have SNI, though this is probably not as significant as hyponatremia occurring in an acute setting.

Understanding both SIADH and CSW is important, because treatment options differ. The mechanism of action is well described in SIADH but remains less clear in CSW. Table 8.2 provides a summary of these two causes of hyponatremia (Moritz and Ayus 2002; Palmer 2003; Ranadive and Rosenthal 2009).

TABLE 8.2 Comparison of syndrome of inappropriate antidiuretic hormone (SIADH) and cerebral salt wasting (CSW)

	SIADH	CSW
Mechanism of action	An inappropriately elevated level of antidiuretic hormone (ADH; also called vasopressin) secreted from the hypothalamus enhances the reabsorption of water from the kidney	Proposed to involve decreased sympathetic input to the kidney (i.e., lack of renin and aldosterone response) and the presence of circulating natriuretic factors (blocking sodium reabsorption in the kidneys)
Causes	Drugs (carbamazepine, oxcarbazepine, SSRIs), acute illness, cortisol deficiency	CNS injury
Extracellular fluid volume	Normal to increased	Decreased
Urine volume	Same or decreased	Same or increased
Heart rate	No change	Increased (tachycardia)
Urine sodium	Increased (>25 mEq/L)	Increased (>25 mEq/L)
Urine osmolality	Increased (>100 mOsm)	Increased (>100 mOsm)
Ratio of urea nitrogen (BUN) to creatinine (Cr)	Normal or decreased	Increased (suggested when the ratio is >20, though more difficult to interpret in children with low muscle mass resulting in a low Cr level)
Treatment	Fluid restriction Demeclocycline: inhibitor of ADH (use with caution, given side effects)	Sodium replacement Fludrocortisone (Florinef): promotes increased reabsorption of sodium from the kidneys (Taplin et al. 2006)

TREATMENT

Decisions about management should factor in the sodium level and whether the child is symptomatic or asymptomatic at that level. Symptomatic hyponatremia, typically at sodium levels of less than 120 to 125 mEq/L, is a medical emergency and is not covered here.

Management includes treating identified causes, such as with glucocorticoid or thyroid hormone replacement. When SIADH is suspected, treatment involves a decrease in the amount of fluids given. When a medication is the cause of SIADH, fluid restriction is often sufficient, allowing the medication to be continued. Demeclocycline is a medication that can block ADH, though it should be used cautiously because it can cause nephrogenic diabetes insipidus, skin reactions, and kidney damage. Most cases of SIADH will improve with fluid restriction. Cerebral salt wasting should be considered when hyponatremia does not improve following fluid restriction. Sodium supplementation should be given when CSW is a possibility and when a restriction in the diet results in low sodium intake.

Other treatment decisions include how essential it is to obtain follow-up sodium levels and what level is considered safe for the child. There is a tendency to check sodium levels too frequently if these factors are not reviewed. As with other alterations from "normal," children who have SNI benefit from care plans that define and document what is considered an acceptable sodium level. For these children, a level at or above 130 mEq/L can be safe. If such a level is established and documented, unnecessary testing can be avoided when a physician who is not familiar with the child encounters an "abnormal" sodium level that is not significant for that child.

SUMMARY OF HYPONATREMIA AND ITS MANAGEMENT

- Hyponatremia is defined as a serum sodium (Na+) level of less than 135 mEq/L, but it typically does not result in symptoms until it is below 125 mEq/L.
- When hyponatremia is identified in a child who has SNI, there are several causes to consider:
  - — SIADH as a result of medications: carbamazepine, oxcarbazepine, and SSRIs
  - — SIADH as a result of an acute event: pneumonia or hydrocephalus (in a child with a ventriculoperitoneal shunt)
  - — Thiazide diuretics
  - — Glucocorticoid deficiency and/or hypothyroidism, as a result of hypothalamic or pituitary dysfunction; testing involves obtaining free T4, TSH, and early morning (8 a.m.) cortisol levels
  - — Cerebral salt wasting
  - — Low sodium intake as a result of severe restriction in the total volume of formula so as to minimize excessive weight gain

- Treatment of hyponatremia in the asymptomatic child who has SNI includes fluid restriction and/or sodium supplementation, as well as treating any identified cause.
- A child may have several contributing problems.
- Fluid restriction: Hyponatremia resulting from medications that cause SIADH can usually be managed with a decrease in total fluids given:
  - This involves calculating an amount that is 65% to 75% of the calculated "maintenance" fluids.
  - As examples, in a child weighing 20 kg (44 lb), this restriction in fluids would be a total daily fluid intake (formula plus water) of 975 to 1125 mL; in an older child weighing 50 kg (110 lb) or more, this would be a total daily intake of approximately 1,400 to 1,600 mL.
  - It is helpful to remember that fluid intake, as estimated by weight, overestimates needs for some children who have SNI, such as children with low metabolic rates, as reviewed in chapter 5 (see "'Required' fluids and nutrition").
  - It is important to include in the calculation all fluid given, including water flushes after feeds and medications.
- Sodium supplementation or replacement with table salt: 1 teaspoon (tsp) of table salt = 2,300 mg of sodium or 100 mEq:
  - Typical daily sodium intake is 1 to 2 mEq/kg; the maximum weight for calculation is 50 kg (50 to 100 mEq daily).
  - For context, the recommendation for adults is to take in less than 2,300 mg of sodium per day, or 100 mEq/day, so as to avoid the adverse effect of a high-salt diet.
  - Decreased sodium intake as a consideration: For an older child (40 kg) receiving 600 mL of formula so as to minimize excessive weight gain, this volume is calculated to provide 22 mEq of sodium per day (the sodium content of formula varies); adding one-half of a teaspoon of table salt would provide an additional 50 mEq of sodium. The urine sodium will be less than 20 mEq/L if this is the only explanation for hyponatremia.
  - Increased sodium excretion (causing higher sodium needs) as a consideration: Some children benefit from a trial of sodium supplementation when CSW is suggested, such as when the urine sodium is more than 20 mEq/L but hyponatremia does not improve with fluid restriction and no other causes have been identified.

- Routine sodium levels need not be obtained once an intervention has helped stabilize the sodium level at close to 135 mEq/L; some children may have a sodium level that is intermittently 128 to 132 mEq/L.
- Symptoms start to occur when the level is below 125 mEq/L; neurological symptoms most often occur with even lower levels, typically less than 115 mEq/L; symptoms can include vomiting, lethargy, restlessness, irritability, muscle spasms, and seizures.
- Parents need to know about the symptoms that can signal a need to check the child's serum sodium level.

Chris is a 19-year-old who has SNI, indicated as cerebral palsy. Routine lab tests identify a serum sodium level of 130 mEq/L and a repeat level, the next day, of 128 mEq/L. His sodium levels over the past year have been 136 and 137 mEq/L. Chris has remained healthy during the past year, with no changes from his baseline noted at the time of these lab tests. He is not taking any medications associated with SIADH. His fluid intake is approximately 2,000 mL and has remained the same over the past year. Free T4 and TSH levels are normal, and the early morning cortisol level is greater than 10 µg/dL (13 µg/dL). There is no noticeable change in his frequency of voiding. His formula volume was decreased three times over the past year, with a goal to avoid excessive weight gain. His dietary sodium intake is currently 15 mEq, compared with 27 mEq one year ago. To increase his sodium intake, ½ tsp of table salt is added to his daily G-tube feeds. His repeat sodium level 1 week later is 133 mEq/mL, with insufficient sodium intake considered the likely explanation for his mild hyponatremia.

High sodium: hypernatremia

Hypernatremia, an elevated sodium level, is typically a result of excessive water loss from the body. One cause is diabetes insipidus (DI), a condition that results from insufficient production of ADH (also called arginine vasopressin, AVP), the hormone involved in the body's retention of water in the kidneys. In children unable to report thirst, excessive urine production is one of the most common symptoms of DI. Other symptoms include lethargy and irritability initially, with seizures at higher sodium levels, especially when the elevation occurs acutely. Symptoms typically do not develop until the serum sodium level exceeds 155 mEq/L.

Children with severe injury or malformations of the central nervous system are at risk for DI when the area of the hypothalamus that releases ADH is damaged (Wang, Cohen, and Duffner 1994). The rate of DI is higher for children with midline malformations, such as children who have holoprosencephaly (Hahn, Hahn, and Kammann 2005). Some children are noted to have stable, asymptomatic hypernatremia, with sodium levels remaining at 148 to 153 mEq/L without treatment (Levey et al. 2010). When DI is suspected, evaluation by an endocrinologist is generally appropriate, with other endocrine disorders also being considered. Treatment may include desmopressin (DDAVP), a synthetic replacement for vasopressin (ADH). Carbamazepine and oxcarbazepine may "treat" partial DI in a few patients, though sometimes the beneficial effect is not evident until the anticonvulsant is discontinued.

Hypothyroidism

Hypothyroidism is low thyroid function. Children who have SNI are at risk for hypothyroidism as a result of hypothalamic or pituitary dysfunction. The hypothalamus produces thyrotropin-releasing hormone, which stimulates the release of thyroid-stimulating hormone from the pituitary gland. TSH, in turn, stimulates the production of thyroid hormone (thyroxine) from the thyroid gland.

Many of the symptoms associated with hypothyroidism are nonspecific and can be seen for other reasons in children who have SNI. Thus it is important to consider annual screening for hypothyroidism. Symptoms associated with hypothyroidism include constipation, low heart rate, cold intolerance, tiredness, and delayed puberty.

Testing for hypothyroidism entails measuring blood levels of free T4 (thyroxine) and TSH (Carrozza et al. 1999). When the free T4 level is low, treatment involves hormone replacement with levothyroxine (Synthroid). Once treatment is initiated or the dose is changed, blood levels are measured again after 4 to 8 weeks to confirm an adequate dose and to avoid an excessive amount of hormone replacement. When hypothyroidism is identified, an 8 a.m. cortisol level should be obtained to assess for central impairment of glucocorticoid secretion.

Growth hormone deficiency

Any child with an endocrine problem that originates from the hypothalamus or pituitary gland, such as hypothyroidism, glucocorticoid deficiency,

or precocious puberty, is also at risk for growth hormone (GH) deficiency. GH deficiency can result from a lack of GHRH secretion by the hypothalamus or GH secretion by the pituitary gland. The most common problems associated with GH deficiency include a decrease in the child's height/length and a delay in the development of puberty.

Treatment involves daily to weekly injections of growth hormone. However, parents may not want this treatment for their child, because it may be preferable to restrict the growth of a child who is dependent on others for transfers. Thus, before pursuing any tests for GH deficiency, it is better to ask, "What will we do with the information?"

GROWTH AND NUTRITION: TOO MUCH AND TOO LITTLE

Growth and nutrition are universal problems for children who have SNI. Initially, the worry is whether the child is getting adequate nutrition. When a gastrostomy feeding tube (G tube) is placed to assist with nutrition, the problem can then shift to excessive growth. The goal is to balance sufficient nutrition for health with growth that does not become excessive. This balance reflects the known risks associated with being chronically undernourished, such as increased susceptibility to infection, and the less recognized risks of excessive growth in children who remain dependent on others for all their needs.

Evaluating undernourishment in children who have SNI relies on what we know about typically developing children. One must be circumspect in applying this information to children who have SNI, for several reasons:

- Muscle mass is often decreased in children who have SNI, resulting in an overestimation of nutritional risk based on weight for age and weight for height/length.
- Weight-for-height proportions are derived from charts for normally developing children.
- Weight gain in children who have SNI often reflects a greater proportion of increased fat deposit than protein mass.
- It is not clear whether children with SNI who are bigger are healthier because of better nutrition or are bigger and healthier because they have fewer problems that compromise health.

Fortunately, there is now a greater recognition of the risk of insufficient nutrition for children who have SNI, along with better monitoring for this condition. This may mean that more children are benefiting from inter-

ventions such as oral formula supplementation or placement of a G tube, and that more children never experience sustained malnutrition.

Assessing nutrition and growth

Nutrition is the process by which a person takes in and utilizes food. Nutrition that is adequate will meet the needs of the cells in the body, allowing maintenance of health and expected growth. Nutrients that the body needs to acquire from food can be broken down into six categories: proteins, carbohydrates, fats, fiber, vitamins and minerals, and water. Proteins, carbohydrates, and fats are often referred to as macronutrients, and vitamins and minerals as micronutrients. The ability to take in and utilize sufficient nutrition is most commonly monitored in children by measuring growth of the body over time.

The goal of growth measurements in children who have SNI is to assess for the risk of inadequate nutrition (malnutrition). In contrast, the goals of growth assessment in normally developing children are to screen for growth as a marker for underlying disease and to maximize a child's potential to achieve normal height and weight standards as an adult. This second goal is often not a desired goal for children who have SNI, as is made more evident in recent articles discussing the option of growth attenuation for these children.

Measuring growth in children who have SNI certainly has its challenges. Many children have substandard growth in both weight and length compared with normally developing children of the same age, so it is often not possible to assess growth as an indicator of nutrition, based solely on the child's weight. Instead, the proportion of weight to height/length is used to monitor a child's nutritional status. Obtaining a length is difficult, however, if the child has contractures or scoliosis. Measures used to assess nutrition can be broken down into several types:

- Ratio of body weight to height/length, using the weight-for-height percentile or body mass index (BMI)
- Methods that indirectly measure height
- Other anthropometric measures (such as comparative measures of the body) that can assist with assessment of nutrition

Measuring length

Though a measured length may be inaccurate, it remains a reasonable approximation for the purpose of monitoring growth over time, including

comparing weight to length. Alternative methods of estimating body length have been identified, though are probably not needed for routine monitoring of growth. These alternative methods, which have been used to estimate height in children with cerebral palsy, include measuring knee height and tibial length (Hogan 1999; Stevenson 1995).

The knee height is measured with the knee and ankle each bent to a 90-degree angle. A Mediform sliding caliper is then used to measure the distance from the heel to the anterior surface of the thigh over the femoral condyles. The formula for calculating body length/height from knee height (KH, in centimeters) is: stature (centimeters) = $2.69 \times KH + 24.2$. The tibial length is measured from the superomedial edge of the tibia to the inferior edge of the medial malleolus by means of a flexible steel tape. The formula using tibial length (TL, in centimeters) is: stature (centimeters) = $3.26 \times TL + 30.8$ (Stevenson 1995). The knee height formula was more recently applied to a group of children with CP, and the calculated body height was found to vary by as much as 12.7 cm (10%) below to 11.8 cm (9%) above actual measured stature (Bell and Davies 2006).

Other anthropometric measures

Comparative measures, called anthropometric measures, of the body are used to assess nutritional status, in addition to weight-for-length percentile or BMI. These measures include triceps skinfold and mid-upper-arm circumference. These measurements have been defined for typically developing children and adults; when applied to children who have SNI, they may overestimate the risk of poor nutrition.

Some growth measurements have been found to significantly underestimate the amount of body fat in children who have SNI. These measurements include weight-for-height percentile, BMI, triceps skinfold, and mid-upper-arm circumference. In one study, BMI significantly underestimated the percentage of body fat in children with CP, as measured by DXA scan. Of the group assessed to have excess body fat by DXA, BMI would have identified 11% to have low body fat (BMI of <10% for males, <15% for females), 70% to have adequate body fat (BMI of 11% to 25% for males, 16% to 30% for females), and only 19% to have excess body fat (Kuperminc et al. 2010). Similar findings are reported with the classification of body fat by mid-upper-arm circumference and triceps skinfold. These measurements tended to underestimate the percentage of body fat in children with CP, as well as in the reference group—though the underestimation was much greater for the group with CP. Although the children with CP and those in

the reference group had similar levels of body fat as measured by DXA (means 30% and 29%, respectively), those with CP had overall lower *z* scores for BMI, mid-upper-arm circumference, triceps skinfold, and mid-upper-arm fat area than children in the reference group (Kuperminc et al. 2010).

This discrepancy probably reflects the significant muscle wasting that can be seen in children who have SNI, especially in the extremities (Kong and Wong 2005). For reference, the legs make up about 25% of an average person's weight. An average adult male body is 42% skeletal muscle, and an average adult female, 36%, as a percentage of body mass. To a much smaller degree, low bone density, as frequently identified in children who have SNI, may also contribute to the discrepancy in measurements. All of this can result in a weight-for-height percentile or BMI that overestimates when a child who has SNI is at risk for being undernourished.

It is important to consider this newer information when interpreting earlier studies. As an example, a retrospective review of anthropometric data for children with CP found that using a weight-for-length percentile of less than 10% "failed" to identify 45% of children with depleted fat stores, as measured by mid-upper-arm fat area—calculated using arm circumference and triceps skinfold thickness—whereas the triceps skinfold measure identified 96% of malnourished children (Samson-Fang and Stevenson 2000).

One study observed that children with moderate to severe CP and greater growth, as assessed by measures including knee height, skinfolds, and arm muscle area, had better health, as assessed by the number of recent healthcare visits and days of missed school (Stevenson et al. 2006). What this study does not tell us is whether such children are healthier because they are bigger or are bigger because they are in better health as a result of less compromise to health.

Blood tests

Lab tests have a limited role in nutrition assessment. Some tests can measure for specific deficiencies. Iron deficiency, for example, is measured with a complete blood cell count and iron studies. Measures of liver protein levels, including prealbumin and albumin, have less of a role than originally believed.

A prealbumin level is better at indicating adults at risk for poor health and nutrition, rather than as a test for malnutrition. The prealbumin level

may correlate more with the underlying disease than with the anthropometric measures of malnutrition. Albumin is not seen as having a role in the assessment and monitoring of nutritional status (Myron Johnson et al. 2007; Shenkin 2006). Few studies have looked at prealbumin and albumin as indicators of nutritional status in children who have SNI. In a study of children with CP, these measures did not correlate with nutritional assessment, though there was, once again, the challenge of using anthropometric measures that may have overestimated malnutrition in the children in this study (Lark et al. 2005). Factors that can decrease the prealbumin and albumin levels include inflammation, such as from recurrent infection or chronic inflammation (Fuhrman, Charney, and Mueller 2004).

Dietary history

Physical growth can reflect on the ability of oral intake to meet the body's energy expenditure. A dietary history can estimate other aspects of nutritional intake. Parents and caregivers can keep a 3-day journal of the child's diet, and the journal can then be analyzed by a dietician to assess how well the diet meets the nutritional requirements for protein, vitamin, and mineral intake.

Practical considerations: using this information to monitor nutrition

The information provided here is intended to ensure full knowledge of the options for monitoring nutrition. Until an agreed-upon standard is identified, and despite the challenges with measuring height, monitoring a child's weight-for-length percentile or BMI is probably adequate for making a general assessment of nutrition and the risk of inadequate intake. When monitoring the growth of children who have SNI, it is important to be mindful of the studies indicating that weight for length and BMI can underestimate the percentage of body fat in this population. By monitoring information over time, it is generally possible to make a general assessment of whether a child has (1) adequate nutrition, (2) borderline nutrition, or (3) insufficient nutrition:

- How do weight gain measurements compare over time?
- How do weight-for-length percentile or BMI measurements compare over time? Is the percentile staying the same or is it gradually decreasing?
- How is the child doing in general?

- What is the estimated nutritional intake from the child's dietary history?

In addition to a general assessment of nutrition, other information is beneficial when considering a child's current and future risk and the potential benefit from a G tube:

- How much effort and time are required to provide nutrition by mouth?
- Are there any associated symptoms with eating? Is there choking, gagging, coughing, or sputtering during oral feeding?
- Has a videofluoroscopic swallow (VSS) study been done to assess for aspiration, and if so, how recently?
- What is the child's health history? Is there a history of respiratory illness?

SNI and calorie requirements

Children and adults who have SNI commonly have lower energy expenditure as assessed by indirect calorimetry—lower than the estimates using available equations (Azcue et al. 1996; Bandini et al. 1995). In a study of tube-fed adults with severe neurodevelopmental disabilities, the mean resting energy expenditure, as assessed by indirect calorimetric measurements, was 888 ± 176 kcal/day (Dickerson et al. 1999). This translates to three to four cans of 1 kcal/mL formula. The nonbasal energy expenditure (such as from physical activity and spasticity) of children with spastic quadriplegic CP was much lower than that of the typically developing control group (Stallings et al. 1996).

Taking into account this decrease in energy expenditure, children with severe CP were fed a low-energy (0.75 kcal/mL), micronutrient-complete, high-fiber enteral formula through a G tube. The children continued to grow, even with energy intakes of approximately 50% of the estimated average requirements, but without a disproportionate rise in fat mass (Vernon-Roberts et al. 2010). In addition, the majority of micronutrient levels remained within the reference range.

Hypothermia is a significant factor that can further lower the metabolic rate for children and adults who have SNI. Of four adults with chronic central hypothermia, all had a lower resting metabolic rate, and two had no increase in metabolic rate when hypothermic (MacKenzie et al. 1991). These adults also had a higher percentage of body fat, despite similarities

in age, height, and weight, compared with the control group. In a study assessing the mean resting energy expenditure by indirect calorimetry in adults with CP and chronic hypothermia, the energy intake necessary to achieve desired weight changes was restrictive when compared with the basal energy expenditure, often less than 750 kcal/day—less than three cans of 1 kcal/mL formula (Dickerson et al. 2003).

Other factors that can lower metabolic rate include inactivity and an intrathecal baclofen (ITB) pump. Lack of spontaneous upper extremity movement in adults with SNI resulted in a 28% lower measured energy expenditure than in those with preservation of upper extremity movement (Dickerson et al. 2002). For children with cerebral-origin spasticity, increased weight-gain velocity was prevalent in those receiving ITB therapy—a welcome outcome for the underweight child, but increasing the risk of excessive weight gain for others (Bottanelli et al. 2004; McCoy et al. 2006).

In general, the use of tube feeding for children with CP is also associated with a greater deposition of body fat, along with lower muscle mass, compared with typically developing children (Arrowsmith et al. 2010; Stallings et al. 1995; Sullivan et al. 2006). Body fat composition, as measured by DXA, was highest in those with the lowest functional level, as indicated by the Gross Motor Function Classification System (GMFCS), with level III indicating the ability to ambulate with assistance and level V indicating no ambulation even with assistance. In children with GMFCS level III, body fat composition was 24.4%; with level IV, 28.1%; and with level V, 31.3% (Kuperminc et al. 2010).

Protein and micronutrient requirements

The protein and micronutrient needs of children who have SNI are generally similar to the needs of typically developing children (Marchand, Motil, and NASPGHAN Committee 2006; Mascarenhas, Meyers, and Konek 2008). In the absence of evidence-based nutrient allowances for children with neurological impairment, the dietary reference intake (DRI) for protein, vitamins, and minerals for healthy children is recommended. As reviewed earlier, the risk of vitamin D deficiency as a result of limited sun exposure or antiepileptic drugs must be taken into account.

Problems occur when the total intake is insufficient for need or when children who have SNI and a feeding tube require lower energy intakes. Supplementing nutrition by mouth or by feeding tube can correct these deficiencies when oral intake is insufficient. When tube feedings need to

be restricted to avoid excessive weight gain, micronutrients (multivitamin, calcium, and phosphorus) and protein (ProMod or ProCel protein powder) can be provided, as needed. As a general rule of thumb, supplementation becomes necessary when a child is receiving less than four cans (960 mL) of 1 kcal/mL formula.

Interventions to improve or maintain adequate nutrition

Interventions to prevent or to manage malnutrition include the following (Arvedson 2008; Schwarz et al. 2001):

- *Treatment of associated problems* that can contribute to the malnutrition, including constipation, gastroesophageal reflux disease (to decrease food refusal due to esophagitis), and visceral hyperalgesia / central pain (see chapter 5)
- *Feeding therapy interventions*, as determined by speech-language evaluation and VSS, such as thickening of liquids
- *Oral supplementation of energy needs*, including calorie-dense foods, calorie-dense supplements (Resource, Benecalorie), or a formula with 1 kcal/mL
- *Vitamin supplementation*, including multivitamin, calcium, and vitamin D
- *Feeding tube placement*, including temporary use of a nasogastric (NG) tube and placement of a G tube.

Decision to place a gastrostomy feeding tube

Gastrostomy tube feeding is commonly used for children who have SNI, to circumvent oral motor dysfunction, including dysphagia (swallowing difficulties) and pulmonary aspiration, as well as to prevent complications from malnutrition. If malnutrition is severe enough, it can increase the risk of infection, skin breakdown, and poor wound healing.

The decision to place a feeding tube is stressful for parents, for many reasons: further recognition of what is "different" or "impaired" in their child, a sense of failure to feed their child, the need to try harder so as not to give up too soon, or feeling guilty for considering a feeding tube to make feedings "easier" or "less stressful." Recognizing these concerns has helped the medical community to talk with parents, thoroughly yet with sensitivity, about the option of a feeding tube for a child assessed to be at risk for the problems associated with malnutrition.

Yet, even with this sensitivity to what the parent is experiencing, an unnecessary sense of urgency can arise once the concern about adequate nutrition has been identified. With close monitoring of growth, and assuming ready access to medical care in the event of problems such as dehydration or recurrent respiratory illness with aspiration, there is no need to have an exaggerated sense of urgency about this chronic problem. Ongoing dialogue that focuses on balancing the risks and benefits of available options, not on the "need" to do a specific intervention, can improve a parent's confidence in decisions along the way. It is also beneficial to identify goals that may be relevant to such decisions. This may include the goal to continue oral feeding for taste and pleasure, even in the setting of documented aspiration, when parents identify the taste of food as enjoyable for their child. By also recognizing the recent literature reporting the underestimation of fat stores as assessed by weight-for-length and other anthropometric measures, safe and reasonable plans can be made.

Occasionally, parents may refuse a feeding tube for their child, even with the most comprehensive and sensitive follow-up. In these circumstances, palliative care experts and ethics committees can be asked to assess and guide decision making (Isaacs et al. 2004). At times, a referral to child protective services is also considered—but such a referral should be reserved for times when there is concern about parents' decision-making ability or general neglect of the child, rather than implemented for a family that is struggling with decisions about the best interest of their severely impaired child.

Sara, 12 months old, was recently diagnosed with GM1 gangliosidosis. Following several lengthy discussions that included her family, with a focus on their hopes and goals for Sara, the family decides to continue oral feedings. Their primary goal for Sara is to make sure that she remains comfortable throughout her life and to minimize interventions. Oral feedings continue throughout her life. Family and home nurses do not view these feedings as a source of distress or discomfort. Sara's growth remains limited but is not considered harmful in the context of these goals. As her feeding ability decreases, her family adjusts from an amount they think they should give her to an amount that appears to satisfy her.

Sara's family was told she would die by 2 years of age. When Sara is still alive at 30 months, her family seeks a second opinion about her diagnosis. At the clinic visit, where her diagnosis is confirmed, the neurologist indicates that

Sara "needs" a feeding tube as she is "too thin" and at risk for pneumonia. Her family says "we are comfortable with our plan and have no interest in a feeding tube." Sara dies peacefully at home 2 weeks later, surrounded by her family and with support from home hospice.

Sonja, 10 years old, has SNI as a result of hypoxic-ischemic encephalopathy. She is assessed to "need" spinal surgery for severe neuromuscular scoliosis. In addition, a feeding tube is recommended, to improve nutrition before surgery. Child protective services (CPS) is contacted after Sonja's mother misses her clinic appointments with her pediatrician and orthopedic surgeon.

After follow-up, and with agreement from Sonja's mother, a feeding tube is placed. A team meeting with CPS, pediatrics, orthopedics, home care nurse, social worker, palliative care team members, and ethics staff is arranged with Sonja's mother, to discuss the spinal surgery. After another team meeting, follow-up with orthopedics, and two separate meetings with members of the palliative care team, a decision is made to decline surgery. Following these discussions, the overall impression is that Sonja's mother was "avoiding" clinic visits out of fear, not out of "neglect" of her daughter, as she felt "she didn't have a choice." Sonja continues to be fed orally, as her mother believes this is pleasurable for her. Sonja remains well at this time, and her mother is pleased with the care and support they are both receiving.

Once a feeding tube has been placed

Gastrostomy tube feeding is clearly recognized to improve overall weight gain (Mascarenhas, Meyers, and Konek 2008; Sullivan et al. 2005), and weight gain often occurs at a rapid rate. A team approach involving the family, dietician, and physicians can identify a reasonable initial tube-feeding plan by assessing what is the greater risk to the child: ongoing malnutrition, refeeding syndrome (Fuentebella and Kerner 2009), or excessive weight gain. It is now more common to see earlier interventions to minimize or prevent malnutrition, making the risk of malnutrition much less common.

It is as critical to be attentive to preventing excess and unnecessary growth after placement of a feeding tube as it is to monitor for undernutrition prior to placement of the G tube. Risk factors for excessive weight gain in children who have SNI, as reviewed earlier, include hypothermia, limited spontaneous arm and leg movement, and intrathecal baclofen pump.

Information to review with a child's dietician and primary physician

Guidelines for energy requirements have been established for children with cerebral palsy. As examples, energy requirements based on height are 12 to 15 kcal/cm for those who are ambulatory and 10 to 11 kcal/cm for those who are nonambulatory. Some children who have SNI may have even lower energy requirements, needing only 6 to 9 kcal/cm, as a result of other factors that lower the child's energy expenditure (Pohl and Cantrell 2006). Another approach when calculating energy intake is to multiply the resting energy expenditure (REE, in kcal/day) by a physical activity coefficient factor. Some children who have SNI may require a factor of 0.8: energy intake (kcal/day) = REE × 0.8. This is in contrast to a factor of 1.5 to 1.6 for a typically developing, healthy child and a factor of 1.1 for a child who has spastic quadriplegic CP.

Most important, monitoring of weight and weight-for-length status over time provides the best indicator of the amount of formula needed to meet energy requirements. The goal should be to maintain the child's weight-for-length percentile or BMI closer to 10% to 25%, rather than 25% to 50%, especially when recognizing the possibility of excess fat deposition that is underestimated by these measures. If a child is assessed to be gaining weight too rapidly, total calories can be decreased by 10% to 15% or more. When the total volume of formula is decreased as a means to restrict caloric intake, micronutrients (multivitamin, calcium, and phosphorus) and protein (such as ProMod) can be supplemented, as needed.

TAKE-HOME POINTS

- Changes in homeostasis in children who have SNI are probably a result of impairment of the hypothalamus, an area of the central nervous system that is involved in autonomic function and regulation of endocrine function.
- Impairment of the hypothalamus can alter both sleep and arousal.
- Management of sleep disturbances includes evaluating contributing problems, such as pain, dyspnea, medications with paradoxical (opposite to intended) effects, and obstructive sleep apnea.
- Medications for improving sleep include melatonin, sometimes up to a dose of 10 mg or more every evening, especially for children with midline brain defects or with severe visual impairment.

- Selection of other medications used for sleep should be based on other possible contributing factors: clonidine is also used for autonomic dysfunction, and tricyclic antidepressants are also used for neuropathic/central pain and visceral hyperalgesia.
- Benzodiazepines are not recommended for treating sleep disturbance but may have a role for intermittent muscle spasms that contribute to disrupted sleep.
- Hyperthermia can result from impaired central regulation of temperature, can be minimized by avoiding exposure to high temperatures in the environment, and can be managed with cooling strategies, including a fan and cool wet towels.
- Hyperthermia associated with an autonomic storm (with facial flushing, sweating, tachycardia, retching, agitation, arching, and stiffening) may benefit from intermittent use of clonidine or morphine sulfate.
- Complications associated with prolonged hypothermia (body temperature below 95 °F) include acute pancreatitis.
- Hypothermia can be minimized and the body temperature maintained above 94 to 95 °F with the use of a hat, scarf, thick socks, gloves, and blankets.
- Cyproheptadine may offer benefit for some children who have hypothermia that occurs with other features of autonomic dysfunction, such as retching and vomiting.
- Early (precocious) puberty is very commonly a result of altered hypothalamic stimulation of earlier-than-expected pubertal changes (younger than 8 years in girls and younger than 9 years in boys).
- Early puberty is benign if it is confined to breast development (premature thelarche) or development of pubic hair, sometimes accompanied by body odor and acne (premature adrenarche).
- Some parents prefer not to treat precocious puberty, because not treating it will result in a shorter final length/height, which can make it easier to lift and transfer the child.
- Menstrual periods may be decreased or eliminated with the use of combined oral contraceptives or injectable progesterone (Depo-Provera).
- The risk with oral contraceptives is deep vein thrombosis, though this risk is lower for individuals younger than 30 years and with certain types of oral contraceptive: those containing the progesterone norethindrone or levonorgestrel, and those with an estrogen dose of less than 40 μg.

- The risk with injectable Depo-Provera is decreased bone mineral density.
- Medical organizations (AAP, ACOG) recommend the medical management of menses, such as with oral contraceptives, before considering hysterectomy.
- Hysterectomy in a disabled individual unable to provide consent may require a court order, depending on state law.
- The final length/height of a child who has SNI can be decreased by not treating precocious puberty, if it occurs, and possibly with high-dose estrogen, though the outcome, including risk, is unknown.
- Nonambulatory children who have SNI are at risk for osteoporosis (low BMD); other risk factors include antiepileptic medications, lack of sun exposure, and micronutrient deficiency.
- Osteoporosis can be minimized with adequate calcium, phosphorus, and vitamin D intake; by supplementing vitamin D, if the child is taking antiepileptic medications; and by providing weight bearing with a stander.
- Bisphosphonates are used to increase BMD and decrease fracture risk and are considered safe in the short term; however, they are not considered standard therapy for low BMD, and the long-term impact on bone remodeling is unknown.
- Hyponatremia (low serum sodium) can occur with carbamazepine and oxcarbazepine, as a result of syndrome of inappropriate antidiuretic hormone.
- SIADH can also result from glucocorticoid deficiency and hypothyroidism.
- Injury to the central nervous system can result in SIADH and cerebral salt wasting.
- SIADH is most commonly treated by restricting fluids by two-thirds to three-quarters.
- CSW is most commonly treated with sodium replacement.
- The risk for hypothyroidism can be assessed with an annual blood test.
- Monitoring growth—specifically, weight for height/length or BMI—is the best way to monitor a child's nutritional status.
- Weight for height and BMI may underestimate fat stores in children who have SNI, given their reduced muscle mass and bone mineral mass, thereby overestimating the nutritional risk.
- After feeding tube placement, children who have SNI are at significant risk for overfeeding, with subsequent excessive weight gain.

- Children at greatest risk for excessive weight are those who have chronic hypothermia; those who have the least movement, such as limited spontaneous movement of the arms and legs; and those who have an ITB pump to treat spasticity.
- Such children often have a lower energy expenditure than is calculated for a nonambulatory child with cerebral palsy.
- When the volume of formula is decreased to restrict caloric intake, micronutrients (multivitamin, calcium, and phosphorus) and protein (such as ProMod protein supplement powder) can be added, as needed.
- Such supplementation is typically needed when a child receives less than four cans of 1 kcal/mL formula.

References

AAP (American Academy of Pediatrics) Committee on Bioethics. 1999. Sterilization of minors with developmental disabilities. *Pediatrics* 104(2 Pt 1):337–40.

ACOG (American College of Obstetricians and Gynecologists) Committee on Adolescent Health Care. 2009. ACOG Committee Opinion No. 448: menstrual manipulation for adolescents with disabilities. *Obstet Gynecol* 114(6):1428–31.

ACOG Committee on Ethics. 2007. Committee Opinion No. 371: sterilization of women, including those with mental disabilities. *Obstet Gynecol* 110(1):217–20.

Allen DB, Kappy M, Diekema D, Fost N. 2009. Growth-attenuation therapy: principles for practice. *Pediatrics* 123(6):1556–61.

Arrowsmith F, Allen J, Gaskin K, et al. 2010. The effect of gastrostomy tube feeding on body protein and bone mineralization in children with quadriplegic cerebral palsy. *Dev Med Child Neurol* 52(11):1043–47.

Arvedson JC. 2008. Assessment of pediatric dysphagia and feeding disorders: clinical and instrumental approaches. *Dev Disabil Res Rev* 14(2):118–27.

Azcue MP, Zello GA, Levy LD, Pencharz PB. 1996. Energy expenditure and body composition in children with spastic quadriplegic cerebral palsy. *J Pediatr* 129(6): 870–76.

Bachrach SJ, Kecskemethy HH, Harcke HT, et al. 2006. Pamidronate treatment and post-treatment bone density in children with spastic quadriplegic cerebral palsy. *J Clin Densitom* 9(2):167–74.

Bachrach SJ, Kecskemethy HH, Harcke HT, Hossain J. 2010. Decreased fracture incidence after 1 year of pamidronate treatment in children with spastic quadriplegic cerebral palsy. *Dev Med Child Neurol* 52(9):837–42.

Backeljauw PF, Rose SR, Lawson M. 2004. Clinical management of menstruation in adolescent females with developmental delay. *Endocrinologist* 14(2):87–92.

Bandini LG, Puelzl-Quinn H, Morelli JA, Fukagawa NA. 1995. Estimation of energy requirements in persons with severe central nervous system impairment. *J Pediatr* 126(5 Pt 1):828–32.

Bell KL, Davies PS. 2006. Prediction of height from knee height in children with cerebral palsy and non-disabled children. *Ann Hum Biol* 33(4):493–99.

Black DM, Kelly MP, Genant HK, et al., Fracture Intervention Trial Steering Committee, HORIZON Pivotal Fracture Trial Steering Committee. 2010. Bisphosphonates and fractures of the subtrochanteric or diaphyseal femur. *N Engl J Med* 362(19):1761–71.

Bottanelli M, Rubini G, Venturelli V, et al. 2004. Weight and height gain after intrathecal baclofen pump implantation in children with spastic tetraparesis. *Dev Med Child Neurol* 46(11):788–89.

Carrozza V, Csako G, Yanovski JA, et al. 1999. Levothyroxine replacement therapy in central hypothyroidism: a practice report. *Pharmacotherapy* 19(3):349–55.

Caulton JM, Ward KA, Alsop CW, et al. 2004. A randomised controlled trial of standing programme on bone mineral density in non-ambulant children with cerebral palsy. *Arch Dis Child* 89(2):131–35.

Chad KE, Bailey DA, McKay HA, et al. 1999. The effect of a weight-bearing physical activity program on bone mineral content and estimated volumetric density in children with spastic cerebral palsy. *J Pediatr* 135(1):115–17.

Cole JA, Norman H, Doherty M, Walker AM. 2007. Venous thromboembolism, myocardial infarction, and stroke among transdermal contraceptive system users. *Obstet Gynecol* 109(2 Pt 1):339–46.

Collins AM, Danzl DF. 2006. Hypothermia with profound anemia and pancreatitis. *Wilderness Environ Med* 17(1):31–35.

Dickerson RN, Brown RO, Gervasio JG, et al. 1999. Measured energy expenditure of tube-fed patients with severe neurodevelopmental disabilities. *J Am Coll Nutr* 18(1):61–68.

Dickerson RN, Brown RO, Hanna DL, Williams JE. 2002. Effect of upper extremity posturing on measured resting energy expenditure of nonambulatory tube-fed adult patients with severe neurodevelopmental disabilities. *JPEN J Parenter Enteral Nutr* 26(5):278–84.

Dickerson RN, Brown RO, Hanna DL, Williams JE. 2003. Energy requirements of nonambulatory, tube-fed adult patients with cerebral palsy and chronic hypothermia. *Nutrition* 19(9):741–46.

Dizon CD, Allen LM, Ornstein MP. 2005. Menstrual and contraceptive issues among young women with developmental delay: a retrospective review of cases at the Hospital for Sick Children, Toronto. *J Pediatr Adolesc Gynecol* 18(3):157–62.

Dodge NN, Wilson GA. 2001. Melatonin for treatment of sleep disorders in children with developmental disabilities. *J Child Neurol* 16(8):581–84.

Dong X, Leppik IE, White J, Rarick J. 2005. Hyponatremia from oxcarbazepine and carbamazepine. *Neurology* 65(12):1976–78.

Drezner MK. 2004. Treatment of anticonvulsant drug-induced bone disease. *Epilepsy Behav* 5(Suppl 2):S41–47.

Feudtner C. 2011. Growth attenuation: health outcomes and social services. *Hastings Cent Rep* 41(5):4–5; author reply 7–8.

Fuentebella J, Kerner JA. 2009. Refeeding syndrome. *Pediatr Clin North Am* 56(5):1201–10.

Fuhrman MP, Charney P, Mueller CM. 2004. Hepatic proteins and nutrition assessment. *J Am Diet Assoc* 104(8):1258–64.

Gissel T, Poulsen CS, Vestergaard P. 2007. Adverse effects of antiepileptic drugs on bone mineral density in children. *Expert Opin Drug Saf* 6(3):267–78.

Greer FR, Krebs NF, American Academy of Pediatrics Committee on Nutrition. 2006. Optimizing bone health and calcium intakes of infants, children, and adolescents. *Pediatrics* 117(2):578–85.

Gunther DF, Diekema DS. 2006. Attenuating growth in children with profound developmental disability: a new approach to an old dilemma. *Arch Pediatr Adolesc Med* 160(10):1013–17.

Hahn JS, Hahn SM, Kammann H. 2005. Endocrine disorders associated with holoprosencephaly. *J Pediatr Endocrinol Metab* 18(10):935–41.

Hauer JM. 2008. Central hypothermia as a cause of acute pancreatitis in children with neurodevelopmental impairment. *Dev Med Child Neurol* 50(1):68–70.

Henderson RC, Kairalla J, Abbas A, Stevenson RD. 2004. Predicting low bone density in children and young adults with quadriplegic cerebral palsy. *Dev Med Child Neurol* 46(6):416–19.

Henderson RC, Kairalla JA, Barrington JW, et al. 2005. Longitudinal changes in bone density in children and adolescents with moderate to severe cerebral palsy. *J Pediatr* 146(6):769–75.

Henderson RC, Lark RK, Gurka MJ, et al. 2002. Bone density and metabolism in children and adolescents with moderate to severe cerebral palsy. *Pediatrics* 110(1 Pt 1):e5.

Henderson RC, Lark RK, Kecskemethy HH, et al. 2002. Bisphosphonates to treat osteopenia in children with quadriplegic cerebral palsy: a randomized, placebo-controlled clinical trial. *J Pediatr* 141(5):644–51.

Hoebert M, van der Heijden KB, van Geijlswijk IM, Smits MG. 2009. Long-term follow-up of melatonin treatment in children with ADHD and chronic sleep onset insomnia. *J Pineal Res* 47(1):1–7.

Hogan SE. 1999. Knee height as a predictor of recumbent length for individuals with mobility-impaired cerebral palsy. *J Am Coll Nutr* 18(2):201–5.

Holick MF. 2007. Vitamin D deficiency. *N Engl J Med* 357(3):266–81.

Holtmann M, Krause M, Opp J, et al. 2002. Oxcarbazepine-induced hyponatremia and the regulation of serum sodium after replacing carbamazepine with oxcarbazepine in children. *Neuropediatrics* 33(6):298–300.

Huang SM, Chen CC, Chiu PC, et al. 2004. Tuberculous meningitis complicated with hydrocephalus and cerebral salt wasting syndrome in a three-year-old boy. *Pediatr Infect Dis J* 23(9):884–86.

Isaacs D, Kilham HA, Somerville HM, et al. 2004. Nutrition in cerebral palsy. *J Paediatr Child Health* 40(5–6):308–10.

Jacob S, Spinler SA. 2006. Hyponatremia associated with selective serotonin-reuptake inhibitors in older adults. *Ann Pharmacother* 40(9):1618–22.

Jan JE, Freeman RD. 2004. Melatonin therapy for circadian rhythm sleep disorders in children with multiple disabilities: what have we learned in the last decade? *Dev Med Child Neurol* 46(11):776–82.

Jan JE, Owens JA, Weiss MD, et al. 2008. Sleep hygiene for children with neurodevelopmental disabilities. *Pediatrics* 122(6):1343–50.

Jan JE, Wasdell MB, Reiter RJ, et al. 2007. Melatonin therapy of pediatric sleep disorders: recent advances, why it works, who are the candidates and how to treat. *Curr Pediatr Rev* 3(3):214–24.

Jekovec-Vrhovsek M, Kocijancic A, Prezelj J. 2000. Effect of vitamin D and calcium on bone mineral density in children with CP and epilepsy in full-time care. *Dev Med Child Neurol* 42(6):403–5.

Jick S, Kaye JA, Li L, Jick H. 2007. Further results on the risk of nonfatal venous thromboembolism in users of the contraceptive transdermal patch compared to users of oral contraceptives containing norgestimate and 35 microg of ethinyl estradiol. *Contraception* 76(1):4–7.

Kelly BD, Hillery J. 2001. Hyponatremia during carbamazepine therapy in patients with intellectual disability. *J Intellect Disabil Res* 45(Pt 2):152–56.

Kirschner KL, Brashler R, Savage TA. 2007. Ashley X. *Am J Phys Med Rehabil* 86(12): 1023–29.

Kloos RT. 1995. Spontaneous periodic hypothermia. *Medicine (Baltimore)* 74(5):268–80.

Kohrman MH, Carney PR. 2000. Sleep-related disorders in neurologic disease during childhood. *Pediatr Neurol* 23(2):107–13.

Kong CK, Wong HS. 2005. Weight-for-height values and limb anthropometric composition of tube-fed children with quadriplegic cerebral palsy. *Pediatrics* 116(6):e839–45.

Kuperminc MN, Gurka MJ, Bennis JA, et al. 2010. Anthropometric measures: poor predictors of body fat in children with moderate to severe cerebral palsy. *Dev Med Child Neurol* 52(9):824–30.

Kuz GM, Manssourian A. 2005. Carbamazepine-induced hyponatremia: assessment of risk factors. *Ann Pharmacother* 39(11):1943–46.

Lark RK, Williams CL, Stadler D, et al. 2005. Serum prealbumin and albumin concentrations do not reflect nutritional state in children with cerebral palsy. *J Pediatr* 147(5):695–97.

Levey EB, Stashinko E, Clegg NJ, Delgado MR. 2010. Management of children with holoprosencephaly. *Am J Med Genet C Semin Med Genet* 154C(1):183–90.

Liamis G, Milionis HJ, Elisaf M. 2011. Endocrine disorders: causes of hyponatremia not to neglect. *Ann Med* 43(3):179–87.

Lidegaard Ø, Løkkegaard E, Svendsen AL, Agger C. 2009. Hormonal contraception and risk of venous thromboembolism: national follow-up study. *BMJ* 339:b2890.

Lohiya GS, Crinella FM, Tan-Figueroa L, Go S. 2005. Deep vein thrombosis in a tetraparesic patient with mental retardation: case report and review of the literature. *Brain Inj* 19(9):739–42.

Long AC, Krishnamurthy V, Palermo TM. 2008. Sleep disturbances in school-age children with chronic pain. *J Pediatr Psychol* 33(3):258–68.

Machado RB, Fabrini P, Cruz AM, et al. 2004. Clinical and metabolic aspects of the continuous use of a contraceptive association of ethinyl estradiol (30 microg) and gestodene (75 microg). *Contraception* 70(5):365–70.

MacKenzie MA, Hermus AR, Wollersheim HC, et al. 1991. Poikilothermia in man: pathophysiology and clinical implications. *Medicine (Baltimore)* 70(4):257–68.

MacKenzie MA, Schönbaum E, Hermus AR, et al. 1995. Sudomotor function in human poikilothermia. *Neurology* 45(8):1602–7.

MacKenzie MA, Wollersheim HC, Lenders JW, et al. 1996. Skin blood flow and autonomic reactivity in human poikilothermia. *Clin Auton Res* 6(2):91–97.

Marchand V, Motil KJ, NASPGHAN Committee on Nutrition. 2006. Nutrition support for neurologically impaired children: a clinical report of the North American Society

for Pediatric Gastroenterology, Hepatology, and Nutrition. *J Pediatr Gastroenterol Nutr* 43(1):123–35.

Mascarenhas MR, Meyers R, Konek S. 2008. Outpatient nutrition management of the neurologically impaired child. *Nutr Clin Pract* 23(6):597–607.

McCoy AA, Fox MA, Schaubel DE, Ayyangar RN. 2006. Weight gain in children with hypertonia of cerebral origin receiving intrathecal baclofen therapy. *Arch Phys Med Rehabil* 87(11):1503–8.

Metz C, Holzschuh M, Bein T, et al. 1996. Moderate hypothermia in patients with severe head injury: cerebral and extracerebral effects. *J Neurosurg* 85(4):533–41.

Moritz ML, Ayus JC. 2002. Disorders of water metabolism in children: hyponatremia and hypernatremia. *Pediatr Rev* 23(11):371–80.

Myron Johnson A, Merlini G, Sheldon J, Ichihara K, Scientific Division Committee on Plasma Proteins (C-PP), International Federation of Clinical Chemistry and Laboratory Medicine (IFCC). 2007. Clinical indications for plasma protein assays: transthyretin (prealbumin) in inflammation and malnutrition. *Clin Chem Lab Med* 45(3):419–26.

Ozdemir H, Aycan Z, Degerliyurt A, Metin A. 2010. The treatment of cerebral salt wasting with fludrocortisone in a child with lissencephaly. *Turk Neurosurg* 20(1):100–102.

Palmer BF. 2003. Hyponatremia in patients with central nervous system disease: SIADH versus CSW. *Trends Endocrinol Metab* 14(4):182–87.

Pelayo R, Chen W, Monzon S, Guilleminault C. 2004. Pediatric sleep pharmacology: you want to give my kid sleeping pills? *Pediatr Clin N Am* 51(1):117–34.

Pohl JF, Cantrell A. 2006. Gastrointestinal and nutritional issues in cerebral palsy. *Pract Gastroenterol* 29(5):14–22.

Presedo A, Dabney KW, Miller F. 2007. Fractures in patients with cerebral palsy. *J Pediatr Orthop* 27(2):147–53.

Ranadive SA, Rosenthal SM. 2009. Pediatric disorders of water balance. *Endocrinol Metab Clin North Am* 38(4):663–72.

Richardson GS, Zammit G, Wang-Weigand S, Zhang J. 2009. Safety and subjective sleep effects of remelteon administration in adults and older adults with chronic primary insomnia: a 1 year, open-label study. *J Clin Psychiatry* 70(4):467–76.

Rosenfield RL, Lipton RB, Drum ML. 2009. Thelarche, pubarche, and menarche attainment in children with normal and elevated body mass index. *Pediatrics* 123(1):84–88.

Ross C, Davies P, Whitehouse W. 2002. Melatonin treatment for sleep disorders in children with neurodevelopmental disorders: an observational study. *Dev Med Child Neurol* 44(5):339–44.

Rousseau MC, Guillotel B. 2001. Risk factors for deep venous thrombosis in tetraparesic mentally retarded patients. *Brain Inj* 15(12):1041–44.

Ruck J, Chabot G, Rauch F. 2010. Vibration treatment in cerebral palsy: a randomized controlled pilot study. *J Musculoskelet Neuronal Interact* 10(1):77–83.

Ruiz C, Gener B, Garaizar C, Prats JM. 2003. Episodic spontaneous hypothermia: a periodic childhood syndrome. *Pediatr Neurol* 28(4):304–6.

Samson-Fang LJ, Stevenson RD. 2000. Identification of malnutrition in children with cerebral palsy: poor performance of weight-for-height centiles. *Dev Med Child Neurol* 42(3):162–68.

Saper CB, Scammell TE, Lu J. 2005. Hypothalamic regulation of sleep and circadian rhythms. *Nature* 437(7063):1257–63.

Savasi I, Spitzer RF, Allen LM, Ornstein MP. 2009. Menstrual suppression for adolescents with developmental disabilities. *J Pediatr Adolesc Gynecol* 22(3):143–49.

Scher MS. 1998. Applying classification of sleep disorders to children with neurologic conditions. *J Child Neurol* 13(11):525–36.

Schnoes CJ, Kuhn BR, Workman EF, Ellis CR. 2006. Pediatric prescribing practices for clonidine and other pharmacologic agents for children with sleep disturbance. *Clin Pediatr* 45(3):229–38.

Schwartz JR, Roth T. 2008. Neurophysiology of sleep and wakefulness: basic science and clinical implications. *Curr Neuropharmacol* 6(4):367–78.

Schwarz SM, Corredor J, Fisher-Medina J, et al. 2001. Diagnosis and treatment of feeding disorders in children with developmental disabilities. *Pediatrics* 108(3):671–76.

Shenkin A. 2006. Serum prealbumin: is it a marker of nutritional status or of risk of malnutrition? *Clin Chem* 52(12):2177–79.

Sheth RD, Barron TF, Hartlage PL. 1994. Episodic spontaneous hypothermia with hyperhidrosis: implications for pathogenesis. *Pediatr Neurol* 10(1):58–60.

Siddiqi SU, Van Dyke DC, Donohoue P, McBrien DM. 1999. Premature sexual development in individuals with neurodevelopmental disabilities. *Dev Med Child Neurol* 41(6): 392–95.

Stallings VA, Cronk CE, Zemel BS, Charney EB. 1995. Body composition in children with spastic quadriplegic cerebral palsy. *J Pediatr* 126(5 Pt 1):833–39.

Stallings VA, Zemel BS, Davies JC, et al. 1996. Energy expenditure of children and adolescents with severe disabilities: a cerebral palsy model. *Am J Clin Nutr* 64(4):627–34.

Stevenson RD. 1995. Use of segmental measures to estimate stature in children with cerebral palsy. *Arch Pediatr Adolesc Med* 149(6):658–62.

Stevenson RD, Conaway M, Chumlea WC, et al., North American Growth in Cerebral Palsy Study. 2006. Growth and health in children with moderate-to-severe cerebral palsy. *Pediatrics* 118(3):1010–18.

Stigler KA, Posey DJ, McDougle CJ. 2006. Ramelteon for insomnia in two youths with autistic disorder. *J Child Adolesc Psychopharmacol* 12(5):631–36.

Sullivan PB, Alder N, Bachlet AM, et al. 2006. Gastrostomy feeding in cerebral palsy: too much of a good thing? *Dev Med Child Neurol* 48(11):877–82.

Sullivan PB, Juszczak E, Bachlet AM, et al. 2005. Gastrostomy tube feeding in children with cerebral palsy: a prospective, longitudinal study. *Dev Med Child Neurol* 47(2):77–85.

Sund-Levander M, Forsberg C, Wahren LK. 2002. Normal oral, rectal, tympanic and axillary body temperature in adult men and women: a systematic literature review. *Scand J Caring Sci* 16(2):122–28.

Szabadi E. 2006. Drugs for sleep disorders: mechanisms and therapeutic prospects. *Br J Clin Pharmacol* 61(6):761–66.

Taplin CE, Cowell CT, Silink M, Ambler GR. 2006. Fludrocortisone therapy in cerebral salt wasting. *Pediatrics* 118(6):e1904–8.

Totosy de Zepetnek JO, Giangregorio LM, Craven BC. 2009. Whole-body vibration as potential intervention for people with low bone mineral density and osteoporosis: a review. *J Rehabil Res Dev* 46(4):529–42.

van Hylckama Vlieg A, Helmerhorst FM, Vandenbroucke JP, et al. 2009. The venous thrombotic risk of oral contraceptives, effects of oestrogen dose and progestogen type: results of the MEGA case-control study. *BMJ* 339:b2921.

Vernon-Roberts A, Wells J, Grant H, et al. 2010. Gastrostomy feeding in cerebral palsy: enough and no more. *Dev Med Child Neurol* 52(12):1099–105.

Wang LC, Cohen ME, Duffner PK. 1994. Etiologies of central diabetes insipidus in children. *Pediatr Neurol* 11(4):273–77.

Ward L, Tricco AC, Phuong P, et al. 2007. Bisphosphonate therapy for children and adolescents with secondary osteoporosis. *Cochrane Database Syst Rev* (4):CD005324.

Ward T, Mason TB. 2002. Sleep disorders in children. *Nurs Clin North Am* 37:693–706.

Wilfond BS, Miller PS, Korfiatis C, et al., Seattle Growth Attenuation and Ethics Working Group. 2010. Navigating growth attenuation in children with profound disabilities: children's interests, family decision-making, and community concerns. *Hastings Cent Rep* 40(6):27–40.

Worley G, Houlihan CM, Herman-Giddens ME, et al. 2002. Secondary sexual characteristics in children with cerebral palsy and moderate to severe motor impairment: a cross-sectional survey. *Pediatrics* 110(5):897–902.

CHAPTER 9

Decision Making

We are drowning in information, while starving for wisdom. The world henceforth will be run by synthesizers, people able to put together the right information at the right time, think critically about it, and make important choices wisely.
—Edward O. Wilson

So far, this book has described the many ways to provide care and comfort for a child who has severe neurological impairment. This chapter describes the process of decision making, which means deciding which of the available interventions—medical or surgical treatments—that *can* be done are appropriate for a particular child; in other words, deciding what *should* be done.

We know that when decision making goes well, the decision "feels right." Focusing on the process rather than on the decision itself is helpful in reaching a decision that feels right. Focusing on the process is also the best way to help a family feel that the best possible decision has been made. Parents also benefit from learning the guiding principles of decision making when their child is still young, so they can call on these tools when needed. The complex process of decision making is also a dynamic process, one that shifts in response to the circumstances of, and the current need for, a decision and the understanding of the likely outcome.

This chapter is written for parents as the primary audience, but it can also help physicians work with families during the process of decision making. In many ways, this information can also help manage uncertainty.

Decision making is described in a variety of ways; for example:

- The process of reaching a position or opinion or judgment, after consideration

- The process of choosing between alternative courses of action
- The process of mapping the likely consequences of decisions, working out the importance of individual factors, and choosing the best course of action to take
- The process of using clinical expertise, patients' concerns, and evidence gathered from the scientific literature to arrive at a diagnosis and treatment recommendations (this is called evidence-based decision making)

THE GOAL OF DECISION MAKING: INTEGRATING FACTS AND VALUES

Decision making is a process that involves the heart and the mind. Ideally, it entails identifying factual information with minimal bias and integrating the goals, beliefs, and values of a family. Defining a family's goals of care is essential. Only when a family understands the goals of care for their child can they consider whether an intervention will meet these goals, such as improving comfort, slowing a decline in health, and maximizing the proportion of care that is provided in the home. Traditionally, medical decision making has focused on what an intervention can do medically, such as treat a problem and prolong a life; defining goals of care makes it possible *also* to consider how an intervention will enhance or burden that life.

This chapter is both the most challenging and, in some ways, the most important in this book. Without an understanding of the process of decision making, information about medical interventions may be one-dimensional, and families may not be fully informed about the decisions they make. Most families recognize and respect the range of decisions they might make, recognizing, too, that their path may look different from the path chosen by another family.

Treatment decisions: just one part of how a child who has SNI lives

A chapter focusing on treatment decisions, as this chapter does, can create an unbalanced impression of how decisions and problems dominate a child's life. In fact, the opposite can be true. Children who have SNI can thrive for months and sometimes for years between decisions. Between times of making decisions, a child's life can take on a new "routine" that

allows him or her to be actively involved in family events and to attend school, for example.

To put it another way, though this chapter—indeed, this book—focuses on times when a child's life interacts with the medical world, in real life these medical interactions are just one of the many aspects of the child's life. Ideally, this interface with medicine enhances how the child lives rather than defining who the child is.

Medical interventions and treatment decisions: some examples

Parents of children and young adults who have SNI become familiar, over time, with the problems that can affect comfort and health, and the available interventions for these problems. The decisions made by families center around interventions that are intended to maintain health, to restore health, if there has been decline, to minimize further decline, and to improve recovery at times of acute illness. In general, the decisions are about interventions that may benefit health in the future or may provide some immediate benefit at a time of life-threatening illness. These interventions and decisions are highlighted in table 9.1.

The difficulty of decision making for children who have SNI

The most difficult decision is a decision with no "right" or "wrong" answer. Parents must make decisions across a wide spectrum of options.

For some families, decisions focus on a "natural" approach that minimizes "doing to" the child; other families take a "doing for" approach that maximizes use of the interventions available. At the heart of all decisions are the desire to be a "good" parent as choices are considered, the goal to minimize harm to the child, and the need, at times, to minimize poorly informed pressure from family and society. And, of course, surrounding all decisions are the routines and demands of daily life.

THE PROCESS OF DECISION MAKING

Again, decision making is best considered as a process rather than an outcome. Decision making is also best approached as an opportunity to become informed (or to inform), without the need for an immediate decision (except in an emergency). Focusing on making a decision often puts the cart before the horse, puts the decision before the components that factor into the decision have been thought through. This section

TABLE 9.1 Types of interventions and decisions for children who have SNI

Surgical interventions	• Gastrostomy feeding tube (chapter 8) • Nissen fundoplication (chapters 5 and 6) • Tracheotomy (chapter 6) • Intrathecal baclofen pump (chapter 7) • Spinal fusion for scoliosis (chapter 6)
Chronic medical treatment	• Treatment used to minimize decline in health in children with chronic medical conditions
Acute medical treatment	• Interventions used to restore health closer to a prior baseline or to minimize the chance of cardiopulmonary arrest (when the heart and breathing stop) • Noninvasive interventions in the home: mucus mobilization and medications by feeding tube for an acute respiratory exacerbation (figure 6.4), electrolyte solution by feeding tube for vomiting at time of illness • Invasive interventions in the hospital: IV medications and fluids, intubation, cardiopulmonary resuscitation
Resuscitation	• See text discussion "Understanding resuscitation (CPR, DNR, DNI)"
Acute and chronic respiratory support	• Acute or chronic noninvasive ventilation: CPAP or BiPAP (continuous or bilevel positive airway pressure), providing positive airway pressure ventilation to the lungs through a mask over the face • Acute invasive mechanical ventilation: placing a tube into the windpipe (intubation) for short-term mechanical ventilation (support of breathing) • Chronic invasive mechanical ventilation: placement of a tracheotomy • Intermittent artificial ventilation: use of a bag valve mask (Ambu bag) for a child with a tracheostomy, to intermittently expand the lungs
Location of care	• Can evolve, as determined by the goals of care • Examples: reviewing the benefit and harm of repeated hospitalizations, considering the preferred location of care at the end of life (table 9.8)

highlights the elements of the process of decision making, as shown in figure 9.1.

When a decision is being considered, it can be helpful to take a step back and start with a clear understanding of the problem and the options available to manage the problem. Here are some important questions to ask:

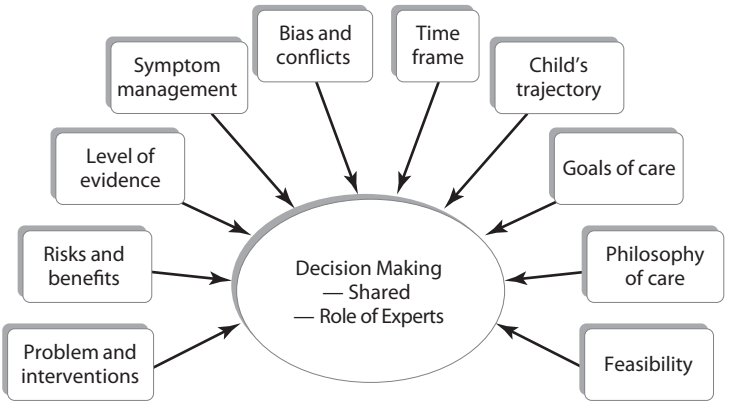


Figure 9.1. Components of decision making

- What is the problem? What interventions/options are available?
  - — How will the outcome look, with and without each option?
  - — What is the level of evidence for each intervention?
  - — What are the potential risks and benefits?
  - — Have all options and alternatives been considered, including the option of not pursuing an invasive intervention?
  - — Are there any conflicts and/or is there any bias influencing the parents/physicians/community? Parents may fear their child will suffer if they do not choose an intervention; physicians may fear harm from symptom treatment; and the community may lack an understanding of the permissible options.
  - — Have distressing symptoms been identified and treated?
  - — What is the time frame for the decision to be made?
  - — What questions need answering?
- What are the values and preferences of the family? What is the philosophy of care?
  - — What personal importance is placed on the benefits and risks of an option (location of care, type of care, the meaning of suffering, treatment of pain, time together as a family, etc.)?
  - — What are the cultural and spiritual beliefs that affect decision making?
  - — Have goals of care been defined?
  - — How does the family approach decision making? How is information shared in the family?
  - — Who is the primary decision maker? Who should be part of this process?

  - What are the fears and hopes of the family?
- Questions of feasibility:
  - What resources exist in the community to support a decision?
  - How will a decision affect the family?

Creating space

Decision making that is challenging needs a "quiet space" beyond the day-to-day care needs and chaos. In the hospital, a sense of urgency can emerge, and the stress of the moment can limit a family's emotional and physical energy. At home, the effort of providing for a child's day-to-day care, along with other responsibilities, can also drain the energy needed for decision making.

Creating an environment of quiet space for decision making can involve several steps, including identifying the time and the individuals needed for a discussion to take place. First of all, parents will feel most settled to "take time" when they know their child's needs are being met. At home, this may mean identifying a team of trusted friends and family to take over some of the day-to-day care for a brief period. Second, a family can identify the individuals they want to involve in discussing a decision. These individuals may include trusted friends and family, the pastor from a family's church, the child's primary pediatrician, specialists in the problems being considered, and members of palliative care teams.

Finally, if things are feeling out of control, it is remarkably helpful to slow things down. Problems that do not require an urgent decision—and that includes most problems—can be mulled over for weeks to months (see table 9.4). Supportive team members can assist with creating time and space for decision making, including identifying the timeline, creating the time, and supporting a calm environment.

Using goals of care as a guide

I want her to be held and loved, involved with family activity, to join us for walks in the park, be with us at the dinner table, part of the family.

Goals of care serve as a guide to decision making. They also help identify points in time to review a child's medical care plan. When that care plan is no longer meeting the identified goals, it is time to revise the plan. Goals of care represent views, beliefs, and values that influence decision

making and plans of care. Here are some examples of goals that may be priorities for different families (Tamburro et al. 2011):

- Maximize comfort
- Minimize suffering
- Maintain health
- Slow the decline in health
- Restore health during acute respiratory illnesses
- Maximize the quality of each day
- Minimize the use of invasive interventions (surgery, procedures, intubation)
- Maximize time together as a family
- Maintain health for an upcoming family event
- Maintain care at home and avoid future hospitalizations

For children who have SNI, it is typical for the family to identify more than one goal. Maintaining health and minimizing discomfort are examples of common goals. Goals of care can also change during the course of a complex, chronic condition. And how goals are prioritized can shift as the ability to meet each goal shifts, as illustrated in figure 1.3. As less benefit is experienced from disease-modifying treatments, the primary goal may shift to improving comfort and not prolonging suffering. Goals may also focus on the location of care, such as when the child experiences less benefit and greater distress from repeated hospitalizations.

Each goal can serve as a guide to decisions. Where a child is along his or her health trajectory can modify goals and guide decisions, as well. A family may decide to limit treatments that have become less successful in restoring the child's health to baseline, or are resulting in increased suffering or prolonging suffering. Such decisions can be made about any treatment, including both invasive interventions such as intubation and more "routine" interventions such as medical fluids and antibiotics (AAP 1994).

What does the family view as important for their child? The answer to this question can provide invaluable guidance with decision making. As often voiced by parents, the answer helps parents know "when I am doing *for* versus doing *to* my child." As an example, a family may identify the following goals: maximize comfort, slow the decline in health, maximize recovery during acute illnesses, and maximize time together as a family. As further decline in health results in more hospitalizations and increas-

ing discomfort, it is natural to redirect care plans toward improving comfort and time together as a family. This can include a decision to focus on care plans that can be accomplished in the home, while avoiding hospitalization for a chronic problem that is now benefiting less from hospital care.

It can be helpful to designate a trusted friend to be an "objective observer" of the identified goals of care. Families can benefit when such a person, as well as trusted members of the medical team, shares his or her observations when critical changes occur. These observations can help a family reflect on the goals of care and consider adjusting the care plan to meet these goals.

Decision making as a philosophy of care

A philosophy of care can be viewed as representing the general values and preferences of a family. As an example, for one family this might mean a desire to provide a child who has SNI with "the best life possible" without the use of surgery or other invasive interventions, when the benefit of these interventions is uncertain. (The exception is an invasive intervention with clearly defined benefit, such as an intervention for a broken bone.) The values and preferences for this family might include the concept that avoiding harm and discomfort is more important than the potential benefit of surgical and invasive interventions, as well as the understanding that focusing on care at home will maximize time together as a family. For another family, the use of interventions that could extend life will be important as a general approach to care for their child. For many families, a middle-of-the-road approach reflects a wish to weigh the pros and cons of each option as problems arise. For these families, goals of care will represent the specific values that can guide decisions at a particular point in time.

For all of these families the process is the same—balancing the benefits and burdens of each approach. Keeping this broader "philosophy" in mind enhances our understanding of the range of approaches taken by families with similar circumstances. As a child's condition changes, the philosophy of care might also change.

Shared decision making

Shared decision making recognizes the need for physicians and families to share information, express preferences, take steps to build consensus toward a decision, and reach an agreement on a treatment plan. This process

increases the medical team's understanding of what is important to the family, decreases uncertainty, limits the overuse of interventions that are not consistent with the identified goals, and can minimize parents' sense of responsibility about the outcome for their child.

In the literature, the importance of shared decision making has focused mostly on adult patients, but many of the principles are relevant for parents of children who have SNI. A recent seminar outlined principles of shared decision making, some of which are summarized here (Salzburg Global Seminar 2010):

- We call on clinicians to
  - — stimulate a two-way flow of information and encourage patients to ask questions, explain their circumstances, and express their personal preferences;
  - — provide accurate information about options and the uncertainties, benefits, and harms of treatment, in line with best practice for risk communication;
  - — tailor information to individual patients' needs and allow them sufficient time to consider their options; and
  - — acknowledge that most decisions do not have to be made immediately, and give patients and their families the resources and help to reach decisions.
- We call on patients to
  - — speak up about their concerns, questions, and what's important to them;
  - — recognize that they have a right to be equal participants in their (or their children's) care; and
  - — seek and use high-quality health information.

Reasons stated for the need for shared decision making include the following:

- Much of the care patients receive is based on the ability and readiness of individual clinicians to provide it, rather than on widely agreed-on standards of best practice or patients' preferences for treatment.
- Clinicians are often slow to recognize the extent to which patients wish to be involved in understanding their health problems, in knowing the options available to them, and in making decisions that take into account their personal preferences.

- Many patients and their families find it difficult to take an active part in healthcare decisions. Some lack the confidence to question health professionals. Many have only a limited understanding about health and its determinants and do not know where to find information that is clear, trustworthy, and easy to understand.

Considering the level of evidence for an intervention

Families don't need to be experts on evidence-based medicine (EBM), but it is helpful to know what physicians mean when they talk about "evidence" in the medical literature. Evidence-based medicine seeks to assess the strength of evidence that helps us understand the risks and benefits of diagnostic tests and of treatments. To accomplish this goal, several categories are used to grade the level of evidence.

Almost all the evidence about interventions for the problems encountered in children who have SNI is from *expert opinion*, the lowest level of evidence, and from *case reports* or *case series*, the second lowest level of evidence. The highest level of evidence is information obtained from *randomized controlled trials* and high-quality *cohort studies*; there are few such studies on children with SNI.

Just because the level of evidence is low, however, does not mean that an intervention will not help. A low level of evidence simply means that there is no strong evidence to indicate, with confidence, that a treatment will help. Rather than meaning to discourage, I share this information on levels of evidence to help readers understand the level of certainty of the information that helps guide decisions. Thus, when an intervention is unintentionally presented as "needed" for an identified problem, rather than as an option to consider, the parent can understand the level of evidence for the benefit of that intervention.

At its best, EBM is a tool that seeks to integrate what we know from the evidence with the expertise of physicians and the values of families. Ideally, this process can help clarify the intended and anticipated outcome from an intervention, as well as help in considering all possible outcomes.

Informed consent

In the process of informed consent, the doctor is required to disclose the pros and cons of an intervention and to review alternatives. This process is most often used for surgical interventions. It is designed to ensure that

families are fully informed about the options and have confirmed their understanding of this information.

There are barriers that interfere with providing informed consent, as highlighted by the following statement: "Providers may consciously or unconsciously impart their own views through their framing of facts, potential outcomes, options, and recommendations to obtain decisions aligned with their own beliefs and values. Many ICUs, hospitals, and geographic regions have their own treatment 'signatures,' reflecting historical norms and entrenched practice patterns" (Holloway and Quill 2010). These barriers can result in a narrow view—for example, the view that a problem "needs" to be treated or the view that some choices are "giving up," are "too aggressive," or are not "morally" appropriate. A common narrow view is that treatment of dyspnea with morphine will hasten death, which simply reflects a lack of training and knowledge in this area.

Indeed, when a narrow view is presented, it often reflects a lack of knowledge in areas of expertise outside the suggested option. Such bias often is not intentional but rather shows a lack of awareness. A team approach can minimize the impact of individual bias. It can also lessen the burden that a parent and an individual physician can feel when grappling with a challenging decision. The goal is to minimize the biases that often frame how information is presented to families.

The influence of bias

Bias can occur on many levels, including assumptions about what it means to have a child who has SNI or a view that an intervention must be used. Bias can reflect a lack of knowledge in certain areas, as noted above, as well as a difficulty handling uncertainty, a desire to provide something of benefit, and the distress of feeling "there is nothing more we can do." There are several aspects of bias:

- The bias of language: the frequent use of *doing something* versus *not treating* if an intervention is not pursued (even though forgoing an intervention such as surgery does not mean other treatments won't be used); the common use of *need* or *require*
- The view that "not doing" is the same as "giving up," and that "doing something" is better than "doing nothing"
- Overstating the benefit indicated by the evidence in the literature—probably not intentionally done, but reflecting the desire to provide an option that is beneficial

- The assumption that interventions will prolong life, and the fear that focusing on the treatment of pain and respiratory distress will hasten death
- Given the multiple healthcare professionals that are often involved, the potential for conflicting information about benefits and risks

Here are several steps that can minimize the influence of bias:

1. *Reframe the language of "treat" versus "not treat" to the language of "provide potential benefit" or "avoid potential harm."* The goal for all parents is to maximize benefit and minimize unnecessary harm; when an outcome is uncertain, the decision to "do" reflects a goal to provide potential benefit, and the decision to "not do" reflects a goal to avoid potential harm.
2. *Avoid the word "need."* Interventions without certain benefit should be viewed (or presented) as *options* to consider.
3. *Consider the level of evidence.* Many interventions used for children who have SNI have an intended benefit but lack a level of evidence to indicate a high level of certainty that this benefit will result.
4. *Seek a core team to help process medical information.* This can help minimize any confusion if there is conflicting information from multiple specialists; ideally, the team includes a physician with a broad base of knowledge to weigh the perspectives from different specialists. A core team can also help consider information in the context of a family's goals and values.
5. *Seek expertise in symptom treatment.* This can improve knowledge about symptom treatment options and minimize the unnecessary fear that symptom treatment will hasten a child's death. It can also expand accurate knowledge about all options and can minimize the chance of a decision being made out of fear that the child will suffer or continue to suffer unless a particular intervention is carried out.
6. *Recognize that care will always be provided.* This can minimize the sense of "doing nothing," by emphasizing that care plans will always identify things to "do" that meet the intended goals and protect against interventions that will not meet these goals.

The benefit of support and experts

Parents of children who have SNI experience many complicated emotions and encounter many challenging new tasks, including the challenge of

navigating the medical care and payer systems. Any of these challenges has the potential to interfere with the process of decision making, and parents deserve access to experts to assist in coping with such challenges. The goal is to create a team that can provide support in different domains (emotional, intellectual, and spiritual) and locations (home, school, clinic, and hospital). This team can both support parents as the center of decision making and create a process of shared decision making, thus minimizing parents' feeling that they alone are responsible for their child's outcome, when the outcome is uncertain or life-threatening.

Such a team can assess and understand how the needs of a family and the availability of local resources affect care plans and decisions. There are many components here, which influence one another (Feudtner, Hexem, and Rourke 2011; Hexem, Bosk, and Feudtner 2011):

- *Family:* family structure (family members, patterns of communication, level of cohesion), coping ability, financial worries, and work of care (caregiver tasks, seeking information, learning new skills, determining the tasks to take on, seeking support, self-care, insurance paperwork, scheduling appointments, communicating with physicians, obtaining medical supplies/equipment and medications, health status monitoring, and health crisis management)
- *Local and regional healthcare systems:* home care, clinics, hospitals, respite care, long-term care facilities, and palliative care and hospice programs

Creating this team starts with recognizing the experts who know the child and family best—the parents, other family members, friends, community pastor, and home care nurses, for example. A physician expert can know what the outcome might be, in general, for many children who have SNI, but will not have the same expertise as a parent in recognizing specific details in an individual child.

In addition to physicians with knowledge and expertise in the medical problems being considered, other individuals bring expertise in how emotions, spiritual beliefs, and other areas affect how decisions are weighed (see table 9.2). The goal is to create a team of experts—experts in attending to the needs of the family and experts in areas that have an impact on decision making.

Team members not responsible for the day-to-day medical care are often able to identify questions that frame the current problem. Parents may have unspoken questions: "What will the doctors think?" "Will the care

the doctors provide change if I share that I am considering changing the focus of care?" "Will they think I am giving up on my child?" "Will they think I am fighting too hard for my child?" "I'm not ready for the doctors to stop trying so hard, but I want a chance to think through what we should be doing. Will they think I'm a bad parent?" Parents may worry that they are not even sure what to ask the doctors.

In addition, parents often feel that they need to focus on how well their child will do, so that they do not appear to be giving up. Parents may give the impression of not understanding the concerns or problems, but often they do understand what the physicians are saying yet find it hard to talk about the possibility of their child's ongoing decline or death.

These and other experiences create many stressful feelings, such as guilt, fear of the unknown, and fear of being a "bad parent," that deserve expert support. This support and guidance can "normalize" a parent's sense of being the only one who has such distressing thoughts with a realization that such thoughts are common and come from a loving place. For many families, it is too painful to share some thoughts until a safe space is created. Some families may also worry that they are "playing God" when making decisions about life-sustaining treatment. Emotional and spiritual support can help a family process such feelings and worries.

The overall goal of this process is to assist with identifying what is in the best interest of the child and to minimize distress for the family. There is increasing evidence that doing so can increase confidence, lessen anxiety, lessen anticipatory grief, and enhance later bereavement (Kreichergs et al. 2007).

Families also need assistance with the details to ensure a successful plan. As an example, a goal to maintain care at home and minimize the use of the hospital requires careful attention to how such care can be supported "in the moment." Such details include agreeing on how the parents will access the care team to assist with questions and concerns when they arise.

Table 9.2 summarizes the roles of various disciplines. Palliative care teams are a natural option, as they include experts from a range of disciplines. If a palliative care team is not available in the community, pediatric hospitals have such experts as social workers and child life specialists. These individuals can also assist with finding resources in the local community. In addition to the "experts," other team members may include the family's pastor, a close friend, or other family members. The goal is to identify those individuals who can attend to the "tough" questions, remain objective about the information to review, attend to areas that are important to the family, and provide support throughout the process.

TABLE 9.2 Expert team members to support the needs of the child and the family

Social workers

Social workers assist families with the social, emotional, and financial challenges encountered. They can provide emotional support, psychosocial assessment, and supportive counseling in collaboration with other providers; link to psychosocial and mental health resources in the local community; anticipate legal and financial needs-such as guardianship, government programs that cover some medical expenses, special needs trust-and direct families to appropriate resources.

Child life specialists

Child life specialists support the needs of siblings and other family members. They can assist siblings with the fears of having a sister or brother with complex healthcare needs, assist families with memory making, provide education around typical grief responses of children, and provide bereavement support.

Chaplains

Chaplains support all faith traditions. They can assist with faith traditions and spiritual values that promote healing and hope, support families as they face loss or grief, identify religious and cultural factors that can shape how a family faces illness and suffering, and provide a supportive presence for sick children and their families.

Nurses

Nurses assist with bedside assessment and care. They often provide assessment of pain and other distressing symptoms, work with families to determine what specific features in a nonverbal child indicate specific distressing symptoms such as pain and dyspnea, create a care plan that is "translatable" to other care providers, and listen in "real time" during times of emotional and spiritual distress for families.

Palliative and hospice medical clinicians: physicians and advance practice nurses

Palliative medicine and hospice experts can assist with medical assessment and development of care plans. This can include providing expertise in symptom management, assisting with advance care planning by working with medical teams and families, and assisting with translating goals of care into how medical interventions can or cannot meet those goals.

Adapted and used with permission from J. Hauer and H. W. O'Brien, "Neurologic Diseases," in J. Wolfe, P. S. Hinds, and B. M. Sourkes (eds.), *Textbook of Interdisciplinary Pediatric Palliative Care* (Philadelphia: Elsevier Saunders, 2011), p. 409.

Palliative care and hospice

I know some people think that palliative care and hospice are only for the end of life but they're not. They are there to make your loved one as comfortable as possible and they can provide services that might not otherwise be available to you. (A mother informing a parent support group)

Palliative care is an approach to care that seeks to improve the quality of life for people with life-threatening conditions and their families. Palliative care supports all treatment options, whether disease-modifying or focused on comfort. Hospice care is an extension of this care, with supportive care that can be provided in the home for the child, siblings, and parents. Both are ideally suited to the needs of children who have SNI as families encounter decisions and seek to understand options, including the option of noninvasive care plans in the home.

These teams offer an interdisciplinary approach to care that can enhance the physical well-being of the child who has SNI, as well as the emotional and spiritual well-being of the child and the rest of the family. As an example, hospice programs typically have physicians, nurses, social workers, chaplains, and bereavement staff, as well as volunteers, art therapists, music therapists, and complementary therapists. Some hospice programs can provide a place for care outside the home that allows respite for families.

Conflict

Conflict can arise in the process of determining the "right" thing to do. Conflict can arise between parents, between the medical team and the family, or between members of the medical team. It often occurs when there is something blocking one person from understanding the view held by another person. The divide tends to persist when each person stays stuck in a position of "certainty and rightness." Unfortunately, parents may be left feeling bewildered and distressed. A parent can seek (or can be provided with) an ally to navigate any conflict. The goal is to assist with understanding and overcoming the barriers that maintain the conflict.

Addressing conflict is easier when a person or a process helps to define the area of difference and obtain agreement on that area of difference, even if the conflict cannot be resolved. Acknowledging and validating another's concerns and perspective is an important first step. This approach

is much more productive than discrediting someone's point of view, as can occur unintentionally when physicians remain focused on "facts" because they believe the parents "are in denial" and "need" to understand the information. Validating the concerns and emotions of parents is essential, with time to seek understanding of beliefs, fears, and hopes while providing support for these views throughout the process. This works best when physicians involved in the conflict seek to (or are assisted to) shift from a sense of "certainty" to a position of "curiosity." Curiosity is an important element when seeking to understand the beliefs and views of others. In fact, these and other essential steps can help minimize the misunderstandings that then lead to conflict. (Physicians wishing to facilitate a process of partnering, as well as collaboration in a setting of conflict, are directed to Feudtner 2007, 2011.)

When conflict cannot be resolved, palliative care teams and ethics committees can provide assistance. An ethics committee can answer questions, at a point in time, regarding the reason for conflict; this often does not result in an answer or a solution but, rather, provides a framework for understanding the conflict. A palliative care team provides the added benefit of developing a relationship with the family, an important step to understanding the values and beliefs that guide the family's decisions, along with the ability to give ongoing support.

Team meetings

When a complex problem would benefit from different specialists providing input into a decision, team meetings are often considered. Traditionally, a team first meets to discuss the problem before the family members are present. This pre-meeting often reflects a desire to protect parents from challenging discussions that involve uncertainty. Parents can ask to be present for the entire discussion, however. After all, parents are already living with the uncertainty, and some parents find it helpful to understand what different physicians and specialists are thinking and considering. Having parents present can also avoid their being presented with a "package plan" without knowing all the factors that went into a recommendation or decision. As shared by one parent, "I get it, there is no one right answer. I prefer to hear everything so I can fully understand what each person is thinking. But I have to ask them to pretend that I am not there initially so they don't hold back, because they think it might be too stressful or too much information. I'm already living with the uncertainty and I'm the one who ultimately has to make or agree with a plan."

The role of hope

> *Hope is not the conviction that something will turn out well, but the certainty that something makes sense, regardless of how it turns out.*
>
> —Vaclav Havel

Parents have many hopes for their children. They often balance hoping for what might be with accepting things as they are. Early in a child's life, parents may hope that the child does better than expected developmentally, yet learn to understand and accept the new reality of their child. When medical problems become chronic and worsen, they can hope that more effort will find the answer to improving the problem, yet make decisions not to put their child through more tests that are less likely to change the treatment plan or the outcome.

Hope can also represent what a parent wishes for but does not expect to see. What a parent hopes for can also shift over time, as a child's condition changes. The shift can go from hoping for a long life, to hoping for recovery of health during an acute illness, to hoping for a lessening of suffering as health declines. As the child's condition worsens, parents often simultaneously maintain hope, including wishes for a full recovery, and prepare for an expectation of ongoing decline.

You don't need to prepare for joy. (Parent reflecting on care decisions)

Just as a family can simultaneously consider what they hope for and what they expect, they can ask their child's medical team to clarify what is possible and what is expected. This process was depicted by a research team using four conceptual models for patients with severe chronic obstructive pulmonary disease (COPD) or advanced cancer (Curtis et al. 2008). These four approaches to hoping and preparing, summarized in table 9.3, may help parents articulate their hopes and worries. Knowing what a parent hopes for and fears can help healthcare teams facilitate ongoing discussions.

Physicians often worry about taking away hope or giving false hope. This concern can influence how information is communicated, such as focusing on the worst outcome, to help a family prepare, or overstating the possible benefit from an intervention, to help support hope. The impact of this very human aspect of providing care can be lessened through a careful and honest discussion of what is likely and what is possible. The

TABLE 9.3 Conceptual models for hope and preparing

	Back and forth	I seem to go back and forth between feeling hopeful and being worried.
	Balance	I want to keep things balanced between being hopeful and being worried; I want to be hopeful but I need to stay realistic, and I want information but not too much.
	Ying-yang	I seem to be able to hear bad news and to hold onto hope—and to do both at the same time.
Hope for improved health Hope for other things	Redirect hope	I used to hope that my son would have a long life and remain healthy; now I hope that he will remain comfortable and be with us for an upcoming family reunion.

Source: Adapted from Curtis et al. 2008, figure 1 and table 1, pp. 612, 613.

case of Lauren, at the end of chapter 2, provides an example of giving parents permission to maintain hope while answering their questions in an honest and direct manner.

Considering an outcome that is better than anticipated

There are times of uncertainty when the outcome might actually be better than anticipated by the medical team. This may reflect the difficulty of asking families to anticipate and prepare for two different outcomes. We would all prefer knowing what to help a family prepare for, but confusion arises when these "predictions" do not turn out as planned after an intervention is not used or is discontinued. Is it better to maximize a family's preparedness for different outcomes by reflecting on "What if your child does not do as well as we would want or hope?" Will some families find it distressing to prepare for their child's possible death when it is also indicated that some children do better than anticipated following a decision to not use or to discontinue an intervention?

There is no easy answer to which approach is better for an individual family. The notion "You don't need to prepare for joy" may be the best

reflection on this challenge. This was the response from a father, when the potential of his daughter's death was first discussed and the parents were asked, "Would it be helpful to discuss what if . . . ?" yet it was acknowledged that some children who have SNI recover from what seems to be a terminal respiratory illness. He then added, "But you wouldn't want to be unprepared for what may happen." For both parents, it made sense to make decisions that would both protect their daughter from the harm of a resuscitation and allow them to hold their daughter, but to hope that the outcome might still be better than expected. This allowed the parents to have a child life specialist spend time with their other children, exploring feelings about having a sister who might die and creating memories; the focus was on making memories in the "moment" that would always remain with them, not on preparing for a specific outcome.

For another family, a similar experience was viewed as a "dress rehearsal" when their son survived a severe respiratory illness, which was treated at home with an antibiotic, prednisone, and morphine when respiratory distress was noted. After his initial recovery, they wanted to wait to see whether he returned to his prior baseline, to determine whether it would make sense to "put him through" another treatment course with an antibiotic and prednisone. They were delighted when he "bounced back" to enjoy his interaction with his family, and they felt they were better prepared for what the future would bring.

Some children also do better than anticipated once comfort is improved, even at times when medications are being used to provide comfort at the end of life. In the case of the boy described above, though his severe respiratory distress suggested to the medical team an impending respiratory failure and risk for respiratory arrest, his distress was noticeably lessened with the first dose of morphine sulfate. He was described by his family as more "relaxed and calm," with his respiratory rate dropping from the high 40s to the mid-20s. His family checked his oxygen saturation (routine monitoring had been discontinued, as it was no longer consistent with his goals of care), and they were surprised to find a level of 94%. As discussed in chapter 6 (see "Improved health in some children following symptom treatment"), morphine can decrease respiratory distress and the associated increased work of breathing. This may result in decreased oxygen consumption and improved effectiveness of breathing. Just as medical treatment, such as an antibiotic for pneumonia, can secondarily improve comfort earlier in a child's health trajectory, symptom treatment, such as morphine for dyspnea, may secondarily allow some improvement in health for a period of time.

Considering a child's health trajectory as a guide

For children who have SNI, a decline in health is often a result of the underlying brain impairment, including many of the problems that contribute to recurrent respiratory illness. Such problems include impaired clearance of mucus from the lungs, impaired cough, and aspiration of oral secretions. The goal of chronic and acute interventions, when the underlying problem cannot be removed, is to minimize the decline in health and maximize recovery during acute respiratory illnesses. Reflecting on a child's health trajectory allows parents and other caregivers to recognize an ongoing decline despite maximal medical interventions.

Reviewing the trajectory of a child's health and the quality of each month can assist in several ways. First, it can inform decisions about surgical interventions. If there is a significant decline from a prior baseline, the potential benefit from an intervention is lower and the potential harm greater. This is considered in chapter 6 and summarized in table 6.7.

Second, reviewing the trajectory also helps everyone reflect on the diminishing benefit from the medical treatment available, as well as the increasing risk of a life-threatening event. For example, one study found that the frequency of hospitalization for children with neurological impairment increased significantly in the final year of life (Feudtner, DiGiuseppe, and Neff 2003). Reflecting on a child's trajectory can help identify a time to reassess and prioritize goals. This may include shifting from a goal of maintaining health to a primary goal of improving comfort and not prolonging suffering. Overall, reflecting on a child's trajectory can help identify when to revisit a child's goals and the options to meet those goals.

For families, the effort and busyness of each day do not leave time for reflection, and it is important not to become caught up in monitoring the trajectory. On the other hand, it is helpful to identify and anticipate times when reflecting on a child's trajectory *can* be beneficial, as in the following circumstance:

- Episodes of acute illness and hospitalizations are increasing in frequency.
- The ability to meet the identified goals of care is decreasing.
- Suffering is increasing as a result of pain and other sources of physical distress.
- There is risk for a life-threatening event.
- A potentially life-threatening episode occurs.

Parents can reflect on their child's health over time by considering his or her current baseline and reviewing any decline from a prior baseline, as "none," "a little," or "a lot." Some helpful questions include the following:

- How does your child's health this month compare with that 6 months, 2 years, or 5 years ago?
- How much would you estimate it has declined? Not at all, by 25%, by 50%, or by more than 50%?
- How often each month is your child sick now compared with then?
- How much daily treatment is needed to maintain the current level of health?
- How much does your child enjoy each day now compared with then?
- How often is your child uncomfortable during a week now compared with then?
- How does your child look now compared with previous photos or videos?

Changes that can indicate an irreversible decline in the function of the CNS include increased frequency of low body temperature, low heart rate, and amount of sleep; changes in the pattern of breathing, with intermittent brief pauses; slowing of intestinal motility; cool hands and feet that are mottled or blue; and increasing retching and pain localized to the GI tract. These problems can occur intermittently in children who have SNI. Progressive, irreversible decline is often distinguished by the frequency of the episodes and the development of new features. This is illustrated by the case of Jonathan, at the end of chapter 6. When such changes are noted, it is beneficial to consider "reversible" sources of problems, such as medication toxicity, while simultaneously being mindful that this may be part of a slow, progressive, irreversible decline in CNS function.

The role of time, timelines, and long-term benefit

Most problems do not require an immediate decision. Once a problem is identified, all too quickly the focus can be on "What is your decision?" Identifying a timeline for decision making can help avoid a rush to make a decision. This timeline creates the needed space for the process of decision making. This is especially important in the hospital, a location of care that can create an artificial sense of urgency for all problems, because some do require more immediate interventions.

The goal of creating a timeline is to identify the time frame within which an intervention can still potentially improve the problem. Another way to think of this is, how long do we have before a significant decline in health may occur without the intervention? Medicine is at risk of creating an artificial sense of urgency, out of its responsibility to anticipate the worst and to identify interventions to prevent the worst from happening. In addition, the focus is often on one specific intervention, without equal consideration of other options. Table 9.4 is designed to capture information that can assist with this process. One of the most helpful steps when considering any of the interventions identified in table 9.4 is to slow the process down, if it is feeling rushed, and to let time be an ally.

Considering long-term benefit and harm

Risk and harm are often considered in terms of the potential complications from an intervention. Though considered less often, harm can also include how an intervention does not meet certain goals or creates unintended and unanticipated consequences. Not taking into account the long-term outcome from an intervention can create such unintended problems. The focus is often on what benefit will be provided in the short term, with less focus on the potential for long-term harm.

Luis is a 4-month-old boy, identified soon after birth as having numerous congenital anomalies with no known genetic diagnosis. He was noted also to have difficulty with breathing. Luis's parents are asked what they want done if Luis is unable to safely breathe on his own. They feel overwhelmed, because they don't have an explanation for his breathing problems. They agree to have him intubated, if that time comes, and then to figure out what to do next. Luis is intubated at 3 months of age and remains ventilated several weeks later.

A tracheotomy is highly recommended, as it may help Luis breathe without mechanical ventilation. After this intervention, there is no change 3 weeks later. A plan for home ventilation is discussed. The parents share with the social worker that they aren't sure that this is the "right" thing for Luis. They feel guilty as they struggle with what is "best" for Luis and for the family. A palliative care consultation and further discussions with the medical team help the family sort through decisions. The family lives in a remote part of the state, limiting options for home nursing. They anticipate that one parent would need to stay home, adversely affecting family finances. In addition, Luis's head MRI findings and his lack of development indicate severe neurological impairment. The parents are reassured that it is appropriate to consider the impact of a

decision on all members of the family when making a decision for one member of that family.

The parents believe that the combination of circumstances makes continued use of mechanical support of breathing too burdensome for Luis. This includes that the problem does not seem to be reversible and that there are no short-term options for Luis to get home. "This is not the life we would want for any of our children." The parents wonder what they would have done differently if this information had been part of the conversation when considering the tracheotomy. With support and reframing, they now view the time as an opportunity to get to know and celebrate Luis's life. They are grateful that their other children are able to participate in memory making, with guidance from the child life service. Luis dies in his mother's arms shortly after mechanical ventilation is discontinued.

As Luis's story illustrates, decision making can artificially focus on the most immediate problem, with less time (or no time) spent projecting what the future of that decision might be. The case of Amy (a young woman with intractable seizures and recurrent respiratory exacerbations), in chapter 7, illustrates another aspect of considering long-term goals.

TABLE 9.4 Timeline for considering an intervention and for a time-limited trial of ventilation

Intervention	Timeline*	Other interventions	Comments
Gastrostomy feeding tube (G tube)	Months	• Treatment of problems that can impair oral intake: constipation, gastroesophageal reflux disease, visceral hyperalgesia/central pain • Feeding therapy interventions, such as thickening liquids • Oral supplementation: calorie-dense foods and supplements • Temporary use of a nasogastric (NG) tube	• Many parents say, after placing a G tube, "I wish we had done this sooner" • Growth measurements underestimate fat stores and can overestimate the risk of impaired nutrition • As a child's health declines, tube feedings should be reviewed, such as feeding to comfort instead of to a "required" amount

(continued)

TABLE 9.4 *(continued)*

Intervention	Timeline*	Other interventions	Comments
Nissen fundoplication	Months	• Treatment of other problems that can result in vomiting (chapter 5) • Jejunostomy tube (J tube) outcomes similar to those for Nissen fundoplication • Disadvantage of J tube: clogging, dislodgement, inability to replace at home	• Problems following the Nissen procedure include retching, decreased ability of the stomach to tolerate the same volume of feeding, and pain localized to the abdomen • May decrease respiratory symptoms, though long-term benefit unclear for respiratory exacerbations (pneumonia, aspiration pneumonia)
Spinal fusion for scoliosis	Months	• Thoracolumbosacral orthosis (TLSO) and molded seating supports	• Consider whether scoliosis is the single risk factor for future respiratory decline or is one of multiple contributing factors (see table 6.7)
Surgery for hip dislocation	Months	• Botulinum toxin, medications to minimize spasticity	• Not all children develop pain (Valencia 2010)
Intrathecal baclofen (ITB) pump	Months	• Empirical treatment with gabapentin, clonidine, and/or nortriptyline for pain as a trigger for spasticity	• Risks of complications with the ITB pump include infection and malfunction of the pump
Tracheotomy	Weeks to months	• Assessment for pain as a trigger for spasticity that alters airway tone	• Greater benefit for conditions of airway obstruction (see table 6.7)
Mechanical ventilation	7–14 days†	• Noninvasive positive airway pressure ventilation with BiPAP or CPAP	• See table 9.5

*The period within which an intervention can be considered before a significant compromise to health is likely, unless otherwise noted.

†The timeline for a time-limited trial of mechanical ventilation for acute respiratory decline as a result of chronic respiratory compromise.

Amy's neurologist requested that she be admitted to the hospital if a seizure persisted despite two doses of rectal diazepam. In addition, he requested that she be intubated if treatment of the seizure in the hospital resulted in respiratory failure. In Amy's case, asking the question, "How will treatment of seizures in the hospital prevent a prolonged seizure from happening again?" helped support her mother's goal not to hospitalize Amy if she had a prolonged seizure despite treatment plans in the home, and not to have Amy intubated if she were in the hospital. There was agreement that the short-term ability to stop her seizure and then intubate her if treatment resulted in respiratory depression would not "fix" the problem in the long term and would, in fact, contribute to her suffering. Her mother recognized that some parents would agree with the request of the neurologist, but this was not how she wanted the remainder of Amy's life to be. The overall goals remained maintaining Amy's comfort and maximizing care plans that could be used in the home, even though such care plans have some associated risk.

Medicine often does not do a "good" job of looking at the long-term picture and including such issues early in the process of decision making. This does not reflect a lack of caring, but rather reflects a focus on short-term needs. Several questions that a family might ask can assist with considering long-term outcome:

- Will this intervention remove or "fix" the problem?
- Will the problem return following this intervention and require more hospitalizations?
- Our most important goals for our son right now are improving his health if possible, improving his comfort, and maintaining his care at home. How will this intervention meet these goals?
- What is needed to support the use of this intervention or technology in the home?
- How many children manage to live in a community like ours with this technology? Are there enough resources to support this plan?
- What does a "typical" child's life look like after this intervention, and what is the worst case scenario that we might expect?

The goal is to make sure that families have information that is relevant to a decision. Such information may include taking into account the feasibility and the long-term consequence of any decision, not just the more immediate benefit.

Forgoing, discontinuing, and time-limited trials

Forgoing refers to a decision not to use an intervention; *discontinuing* refers to stopping an intervention that was started. The two are considered ethically, medically, and legally the same. Emotionally, they can feel much different. Team members can help consider these differences while providing emotional support for the family.

Examples include not initiating the use of mechanical ventilation versus discontinuing ventilation. Other examples can be much more "routine," not involving technology, such as using antibiotics for acute respiratory illnesses for many years, and then stopping their use when a child is experiencing prolonged suffering (AAP 1994).

In addition to thinking about what an intervention can do medically, considering the goals of care is an essential step in the decision-making process. The following steps can help when encountering such challenging decisions:

1. Define all the goals that are intended by an intervention.
2. When not to use an intervention (when to forgo): Identify when the use of the intervention would not be likely to meet these goals.
3. When to stop an intervention (when to discontinue): Identify when the continued use of the intervention is no longer meeting these goals, such as contributing to prolonged suffering by prolonging life.

A time-limited trial can be considered if it is unclear whether an intervention will meet the identified goals (Quill and Holloway 2011). This process can be helpful for some families in times of uncertainty. These are times when an intervention may or may not provide medical benefit as well as meet the goals of care. A time-limited trial is an agreement between the medical team and the family to use an intervention over a defined time period. Here are some steps to follow when considering a time-limited trial:

1. Identify the likelihood that an intervention will be a bridge to the child's prior baseline and will meet the goals of care for this child.
2. Define a time period in which the intervention would be expected to meet this goal.
3. Identify the possible benefit and harm from the intervention, in both the short term and the long term.
4. Consider whether the problem is reversible with the intervention or whether it will recur.

5. Consider the possible outcomes without the intervention.
6. Discuss a plan to implement if the hoped-for benefit does not result within the defined time period or if increased suffering occurs (defining end points and anticipating next steps); this plan can be redefined as circumstances change and need not be considered a rigidly defined plan.

Reversible versus recurrent problems

When considering invasive interventions, it is also helpful to think about whether the problem is likely to be reversible or to recur. This is helpful as families consider what they value most for their child. As examples, one family may value the potential benefit of a time-limited trial of mechanical ventilation. Another family may value "protecting" their child from an intervention such as intubation when it will not prevent another respiratory event.

Projecting into the future

When I am gone, people will be paid to love him, and it's not the same. He's had a good life, but I don't want to prolong his life unnecessarily.

Many parents worry about who will care for their child when they are gone. They might say, "We used to worry about our daughter dying too soon. Now we worry about her living too long." As expressed by a member of one family, "I sometimes wish she would 'go' in her sleep. Then we wouldn't need to worry about decisions."

Parents may also encounter increasing sources of suffering in their child as he or she ages. One family shared, "If I knew then what I know now, I think my decisions would have been different. I would have focused more on 'quality' of days and less on 'quantity' of days." Problems that can be seen with increasing frequency as a child who has SNI ages include bone fractures, pain due to degenerative changes in the bones of the hip and spine, skin breakdown (pressure sores), kidney stones, and the need for blood tests to monitor problems. Certainly, such problems can be anticipated, minimized, and managed as they are identified. But they will occur with increasing frequency even with the best of care.

In some ways, this is the hardest circumstance to contemplate, because it involves projecting into the future while considering treatment in the present. Parents often feel guilty about such thoughts, unsure whether

they reflect what is best for them or what is best for their child. As expressed by one family, "We aren't ready for him to die today, we just aren't sure how much it makes sense to put him through spinal surgery that is intended to add years to his life."

Families benefit from knowing they are not alone in their thoughts. Often, focusing on goals of care and an overall philosophy of care can help a family feel settled about their decisions.

Considering family resources

Most parents want to do "everything" for their child. Conflict and distress can arise when decisions for one child can exhaust the family's resources. It can be helpful to recognize that all families have a finite number of resources, which include emotional, physical, and financial reserves. Families often feel obligated to exhaust these resources in pursuing what is "best" for their child.

It is appropriate to consider how the burdens imposed on a family play a role in decision making. This can create conflict and distress for parents: "Are we doing what is best for our child or what is best for us?" The support of a trusted social worker, chaplain, or friend can ease the burden of such thoughts. The following directives, from the United States Conference of Catholic Bishops (2009), may be helpful here: "No person should be obliged to submit to a health care procedure that the person has judged, with a free and informed conscience, not to provide a reasonable hope of benefit without imposing excessive risks and burdens on the patient or excessive expense to family or community." And, "A person may forgo extraordinary or disproportionate means of preserving life. Disproportionate means are those that in the patient's judgment do not offer a reasonable hope of benefit or entail an excessive burden, or impose excessive expense on the family or the community."

Considering surgical risk

Table 9.4 summarizes the surgical interventions that are often considered for children with SNI. These interventions can benefit some children and produce unanticipated, adverse outcomes for others. Some complications are commonly discussed, such as the risk of infection, excessive bleeding, and death. Others are not as commonly recognized but may be important to consider.

One such consideration is the increasing recognition of the neurotoxicity of anesthesia, as a result of neuronal cell death (DiMaggio, Sun, and Li 2011; Flick et al. 2011; Williams 2011). Though this has not been specifically looked at in children who have SNI, parents of such children have described declines in CNS function following anesthesia. These children may have less CNS "reserve" and therefore have more evident features to suggest a deterioration of the CNS following anesthesia. When surgery is pursued, this concern can be reviewed with the anesthesiologist.

The development of postsurgical peripheral neuropathic pain is summarized in chapter 4. This is probably not a common complication, but it has been reported in children who have SNI. Parents have described the development of pain behaviors weeks to months following surgery, with no cause identified (such as infection or changes in surgical-site hardware) to explain the symptoms. Such children can benefit from the use of medications for neuropathic pain.

Other examples of "unanticipated" postsurgical problems include changes in airway and body position following spinal surgery that might be undesirable for the child. And in the hospital, the child may have prolonged mechanical ventilation, resulting in the medical team identifying the "need" for a tracheostomy tube.

As reviewed elsewhere, it can be helpful to consider surgical risk and benefit by reviewing a child's health trajectory and determining whether an intervention will address the single source of the problem or whether the problem has multiple sources that will remain after the procedure. Also, there can be a false sense of security if a child has had no respiratory problems in the prior year. Any child who has SNI and who is receiving daily or intermittent respiratory treatment, or who has a weakened cough, is at increased risk for prolonged respiratory failure following surgery. Respiratory treatment can become "routine" and the child then viewed as "doing well," forgetting that the maintenance of respiratory health is the result of this "routine" medical treatment.

Most important, surgery is not "required" unless there is clear evidence of benefit. In general, the interventions indicated in table 9.4 are not "needed" but can be considered. An awareness of this information on surgical risk can help parents determine when it makes better sense to "provide potential benefit" or to "avoid potential harm," can help prepare them for potential outcomes, and can reduce later regret about a decision.

The expertise and limitations of physicians

Just like parents, physicians want to "do the right thing." Several factors can interfere with this goal. It is the premise of this book that such factors stem from good intent. These factors can include the following:

- The job of medicine is to anticipate problems and to use interventions to prevent these problems from occurring.
- This can create an overemphasis on the worst outcome for all children and the "need" for an intervention to prevent this from happening, even though not all children will have this outcome or benefit from the intervention.
- Medicine involves identifying problems and identifying an available treatment; it is challenging to consider that "not doing" is still doing and can be of greater benefit for some children.
- When an intervention is used and does not result in harm or is observed to have some short-term benefit, there is a natural assumption that the long-term outcome would be worse without the intervention.
- This can create an overemphasis on the long-term benefit of such an intervention.
- As the interventions available for children who have SNI have increased, they have become more "routine" and are now seen as "needed" or "required."
- The responsibility of treating problems can result in an unintended use of language such as *refused* to indicate when an intervention is not used, rather than using the term *declined*.
- A physician might see different families in similar circumstances make different decisions; when a decision is made not to use an intervention, this can create distress—not knowing whether this is denying potential benefit for a child.
- It can be distressing for a medical team to support a plan to "wait and see when the time comes"; this distress is in recognition of the many variables that a medical team cannot control when that time comes, and the goal and desire in medicine to "define a plan."
- Few physicians have received training in the treatment of pain, dyspnea, and other sources of physical distress; education in symptom treatment is a recent addition to medical school and

residency training. An overemphasis on the risk of medications to treat pain and respiratory distress remains. Fortunately, the number of physicians with training in symptom management is growing, both to provide direct care and to train future physicians.
- Uncertainty in medicine is sometimes managed by creating a greater sense of certainty than actually exists.

Discussing these factors here is intended to highlight that, in decision making, all individuals bring to the table both expertise and limitations. Physicians bring the expertise of caring for many children with similar conditions. They can also bring an "objective" view, as families struggle with the emotional impact of making decisions for their child.

In addition, this is a reminder of the various perspectives that we all bring to the table. Physicians may misunderstand a family that is maintaining hope as a family that is in "denial." A family may misunderstand a physician who is reviewing resuscitation as a physician who is "giving up." Addressing this issue of different perspectives can minimize the impact of factors that interfere with understanding and trust, as families and physicians attempt to build trust early in the process.

The overall goal is to enhance shared decision making. Sharing decisions requires an ability to be open to perspectives that others bring to the table. Understanding the benefits and limitations of these perspectives can enhance this goal.

TREATMENT DECISIONS FOR ACUTE AND CHRONIC DECLINE IN HEALTH

Tables 9.1 and 9.4 summarize interventions and decisions that are often considered for children who have SNI. Interventions can be categorized into several types:

- *Surgical interventions:* used to improve a problem or to minimize the decline in health
- *Daily medical treatment:* used to minimize the decline in health or treat an acute illness
- *Intubation:* used at times of respiratory failure or respiratory arrest
- *Resuscitation:* used in an attempt to restart the heart and breathing
- *Mechanical support of breathing:* used in the short term or chronically
- *Location of care:* home or hospital—an important consideration as a child's health and comfort change

Defining goals of care is a beneficial part of decision making. Goals of care enhance and are complementary to the process of considering the medical facts. Evidence and experience influence how we think about the anticipated benefit and harm of an intervention; goals of care influence how we think an intervention will benefit the child. The medical benefit and harm can change when there is a significant decline in health. The goals of care can change when there is a decline in comfort and ability to enjoy each day.

Surgical interventions are covered in earlier chapters, with information summarized in table 9.4. This section focuses on resuscitation, mechanical respiratory support, location of care, and other parts of the care plan. These are inherently distressing topics. Though this distress cannot be eliminated, information can empower parents before they encounter difficult decisions.

Reviewing the care plan

It is appropriate and beneficial to review parts of the medical care plan periodically. Such reviews can take place when there is decreasing benefit or increasing harm from interventions in the treatment plan. Changes can be noted as an ongoing decline in health while using interventions that treat associated problems; a decrease in benefit, with a decline in alertness and level of interaction with others; an increase in harm from an intervention; and/or an increase in overall suffering. This can be a time to revisit how goals of care are prioritized and how treatment care plans are meeting the preferred goals of care.

The shift from benefit gained with interventions to limited benefit, increased harm, or prolonged suffering is often very gradual, occurring over months if not years. Different opinions may arise as to when the "line" has been crossed from benefit to harm. What may help in considering this line is to anticipate what things might look like in the future and to agree that "crossing the line" may be recognized only after reflecting back on the child's trajectory. Some parents have described how they did not fully appreciate the amount of change in their child until they reviewed old photos or videos.

Location of care: hospital versus home

Decisions about treatment can include both what and where. Just as with decisions about medical interventions, decisions about the benefit and

harm of the location of care can help define a care plan. Several questions can be helpful:

- What interventions require hospitalization?
- Has there been decreasing benefit and increasing distress during hospitalizations?
- What is the desired location of care if a child is at risk of dying?
- Does the desired location of care then factor into decisions about forgoing interventions that would require hospitalization?

The role of a hospital is to aggressively evaluate and treat problems. Hospitalization can be beneficial for many and can be potentially burdensome when an ongoing decline in health results in less benefit. Being in the hospital when there has been a significant decline in baseline health can increase the risk of aggressive treatment of an irreversible problem at the end of life. It can be helpful to review the pros and cons of being in the hospital when such a decline in health occurs, when hospitalizations become prolonged, and when they occur more frequently. For some children who have neurological impairment, the frequency of hospitalization increases in the last 9 to 12 months of life (Feudtner, DiGiuseppe, and Neff 2003). An example would be a child who has had an occasional hospitalization, once or twice each year, now being admitted every 2 to 4 months.

In general, interventions that require being in the hospital include initiating mechanical support of breathing; monitoring for respiratory failure, if intubation and ventilation will be used; initiating treatment that cannot be initiated at home (IV treatment, for example); and surgical treatment. For some families, the decision to forgo such treatment options allows a decision not to use the hospital in the future. For other families, observing increasing distress and decreasing benefit for their child when hospitalized helps guide decisions not to initiate interventions, such as IV treatment and resuscitation, that require or result in hospitalization.

Chapter 6 reviews the potential benefit and harm of the hospital versus the home (see also table 9.8), including the option of a respiratory home care plan. The hospital has the benefit of immediate access to diagnostic tests and interventions. When there is a decline in health, however, this access increases the risk of invasive tests and treatments that will not improve the health problems. This can also create an overreliance on information from tests. It can be helpful to reflect back and ask whether the repeated use of tests and interventions in the hospital is proving

beneficial at times of health decline by supporting recovery to an "acceptable" baseline, or whether the tests are becoming more burdensome to the child.

By considering the diminishing benefit to be gained from the hospital, the care team can focus on the feasibility of a care plan in the home. There are several questions to consider:

- Are there distressing symptoms such as pain or dyspnea? If so, how can they be managed?
- What other problems can be improved by treatment? How can they be treated in the home?
- How will a family get answers to their questions as they arise?
- Is there a palliative care team or hospice team in the community to support such a plan?
- Can a pediatric provider work with an adult hospice team to meet the needs of the child and family?

Addressing these questions is essential, as effective home care requires planning and access to a team with the skills to anticipate and manage the concerns and problems that can arise. A parent shouldn't feel responsible for anticipating what will happen; a child's healthcare team can assist with such planning.

A decision not to hospitalize for treatment of chronic, intermittent problems does not prevent a child from being admitted to the hospital. There can still be circumstances in which the child would benefit from being in the hospital, such as management of a broken bone.

When decisions have been made to forgo interventions and a child is hospitalized, having detailed documentation can avoid confusion and interventions that are not consistent with the child's care plan. When their son was admitted for a new, potentially reversible problem, one family said, "We felt like we were thrown to the wolves." For this family, their child's documentation did not explain the goals of care beyond the decision not to intubate or resuscitate. In addition to such documentation, contact information for the team most familiar with the care plan can avoid unintended consequences.

Goals of care can help "ground" a family in decisions that make best sense for their child. Some children who have SNI and are experiencing an ongoing decline in health can benefit from repeated hospitalizations. There can also be an increasing burden to the child and family, however, as dependence on the hospital increases. Each family deserves a support-

ive team that can keep discussions "grounded" in how this location of care is meeting their child's goals of care.

As with other decisions, location of care is best recognized as a fluid process, not a decision set in stone. Considering the benefit and limitation of any intervention, including hospitalization, can increase an awareness that guides later decisions as the child's story continues to unfold.

Location of death

This is a topic that some families may not be ready to consider. Other families will want to think about how this decision can fit into other decisions. Contemplating "how I want my child's last weeks, days, and hours to be" can then factor into decisions about location of care and forgoing interventions. Some families have described the location of death as the final thing they have control over in their child's life.

Giving consideration to location of death is not about predicting when death will occur, but about realizing that the hospital is providing less benefit and is increasing the likelihood that death could occur in an unwanted location. In addition, having the opportunity to plan allows a more fully informed decision about resuscitation and other invasive interventions. Dying in the hospital is often a result of not planning.

In one study reviewing the location of death of children who had cancer, planning resulted in 72% home deaths, versus 8% home deaths for those children whose parents did not plan (Dussel et al. 2009). Parents who planned were also less likely to have preferred a different location of death (2%) than those who did not plan (46%), and to be very comfortable with the location of death (84% versus 40%). The important point of this study is not where death occurs but that a family has an opportunity to identify and plan for the preferred location.

Planning for an acute event versus decisions "in the moment"

Some families feel more settled when they can anticipate and plan. Other families find it unsettling to make such plans. Neither approach is right or wrong. The information provided in this chapter can help both with planning before an event happens and with reflecting on the experience once an event has occurred. A supportive medical care team can help tailor an approach that works best for each family. The case of Kaitlyn, in chapter 6, is an example of being informed and then later making decisions "in the moment."

What is identified or anticipated within a child's care plan can change in the moment. A supportive team can help let the journey unfold, while supporting and informing along the way. Ideally, this is a team that can meet families where they are, not where the team thinks they should be, in the process of decision making.

Understanding resuscitation (CPR, DNR, DNI)

Discussing resuscitation can be a significant source of distress. It is relatively "easy" to discuss in great detail why children who have SNI have respiratory or gastrointestinal problems. In contrast, little time is spent reviewing the details of resuscitation: it is hard information for families to consider, and physicians do not want to be a source of distress by discussing resuscitation. As emphasized elsewhere, reviewing information about resuscitation should be viewed as an opportunity to be informed before needing to make a decision. The information summarized here is intended to enhance this process.

Definitions

These are the terms most commonly used in referring to resuscitation and the circumstances in which it is used:

- *Respiratory arrest* refers to breathing that has stopped.
- *Cardiac arrest* indicates that the heart has stopped (no pulse).
- *Cardiopulmonary resuscitation (CPR)* is an attempt to restart breathing and the heartbeat when a person has stopped breathing or when the heart has stopped, referred to as *cardiopulmonary arrest*. Interventions used during CPR include the following:
  - — Inflating the lungs with a mask over the face or a tube inserted into the windpipe
  - — Repeatedly pushing down very firmly on the chest to mimic the heart's function and cause blood to circulate, referred to as *cardiac compressions*
  - — Using electric shocks in an attempt to correct the rhythm of the heart or to restart the heart, referred to as *electrical cardioversion* (*cardiac shock*)
  - — Using drugs in an attempt to correct the rhythm of the heart or to restart the heart
- *Respiratory failure* indicates that the respiratory function of gas exchange is not adequate. This can result in blood oxygen (O_2) and/

or carbon dioxide (CO_2) levels that are outside the range necessary to support life and avoid complications. Respiratory failure can progress and result in respiratory and cardiac arrest.
- *Intubation* is utilized when respiratory failure may result in respiratory arrest or when respiratory arrest has occurred. A decision to *do not intubate (DNI)* can be made based on the goals of care identified for a child.
- *Do not resuscitate (DNR)* refers to the decision not to use CPR. Decisions about limits on resuscitation do not alter other areas of a child's care plan. DNR is not the same as "comfort care only" (see below). The DNR order is only one component of defining the appropriate intensity of care.
- *Resuscitation status* refers to decisions about resuscitation and intubation. Such decisions are about CPR and intubation only; all other medical care that meets the identified goals of care will be continued.

Other terms that are sometimes used:

- *Do not attempt resuscitation (DNAR)* is the same as DNR; the addition of *attempt* places the emphasis on resuscitation being an attempt at restoring heart function and breathing that often does not have the intended benefit.
- *Allow natural death (AND)* can be used in place of DNR or DNAR. It indicates that treatment is focused on keeping a child comfortable and protecting him or her from treatments that are not likely to have the intended benefit. The term reflects a focus on what is being done rather than on what is being avoided.
- *Comfort care* is another term used to indicate treatment that is focused on maintaining or improving comfort, not on prolonging life.
- *Advance care planning* is planning in advance of an event and can ensure that only the interventions that are agreed upon in advance will be used.

What decisions about resuscitation do and don't mean

Decisions about resuscitation are not about limiting care but about protecting from specific interventions. This point is emphasized to ensure that the focus remains on the intent of the decision. It is natural to worry that a decision not to attempt resuscitation will be viewed as "giving up." *Instead*, such decisions

are about protecting a child from an intervention that will not meet the goals that a treatment, for that child, is intended to meet. Decisions made out of a sense of needing to do "everything" can be minimized when parents and caregivers are reminded that some loving decisions involve protecting a child from the potential harm of medical interventions.

A decision about one area of care does not change care in other areas. This is a critical point, as it is a significant source of distress for parents. Parents often worry that physicians "will not try as hard" if a decision is made to protect their child from the efforts of resuscitation, especially when in the hospital. Confusion may arise if physicians place an emphasis on keeping the child comfortable before understanding whether there are other changes in the care plan. The child's medical team can minimize distress and confusion by ensuring that any treatment that is providing ongoing benefit and meeting the goals of care will be supported and continued.

A decision to forgo resuscitation does not mean that a child is dying. A decision about resuscitation should not be left until a child is dying. For some children, an event can appear life-threatening but the child does not die. An event that a child might not recover from is also an event that resuscitation is less likely to reverse, and for which resuscitation is less likely to result in discharge from the hospital and less likely to allow a return to the prior baseline, with no additional injury.

When to discuss resuscitation

> *We avoided any discussion out of fear. We thought we couldn't face making a decision. But we came to realize that fear of the unknown was far greater than the experience of discussing "what if." Most importantly, discussing was not about a decision to "let our son go" but helped us focus on "how to let him live."*

Many families find that being informed about future decisions is less stressful than worrying about the future. It helps to be reminded that a process that seeks to inform is not the same as making a decision.

It is helpful to identify agreed-upon times to review a child's resuscitation status and, just as important, times when *not* to discuss. Parents of children who have SNI can sometimes feel they are being asked repeatedly to make the same decision when nothing about their child's situation has changed. The following suggestions focus on times when preparing for the risk of a life-threatening event may be essential or when a decline in health and function means there will be declining benefit from interventions:

- Risk for life-threatening event:
  - Risk for respiratory failure in children who have SNI
    - Risk with first respiratory illness/decline/event: no cough, no gag reflex, severe hypotonia, and disordered central breathing with prolonged pauses (central apnea)
    - Risk with future respiratory illness: suggested by increasing use of chronic interventions to maintain respiratory health (see table 6.5), increasing frequency of respiratory exacerbations, declining recovery following acute treatment, and declining baseline respiratory health
  - Risk for sudden unexpected death in children who have SNI: an uncommon event, associated with poorly controlled seizures and conditions that result in disordered breathing with central hypoventilation and apnea (such as Rett syndrome)
  - Risk with recurrent "pseudo-obstruction" of the intestinal tract (Goulet et al. 1999; Heneyke et al. 1999; Jancar and Speller 1994)
- Significant decline in health, decline in alertness and interactiveness with others, and/or increase in suffering: a time to revisit goals of care, how care plans are meeting the goals of care, and how resuscitation fits into those care plans

The goal of anticipating times to review resuscitation status is a way of giving parents and physicians permission to broach the subject. Identifying agreed-upon times can also help ensure that a discussion about resuscitation takes place with an informed and supportive person or team. For some families, this may be a member of the healthcare team most familiar with the child and family. Other families may prefer to have such discussions with experts who are not responsible for the day-to-day medical care of their child, such as palliative care teams.

Equally important, these guidelines can help assure parents that any future discussions will occur because of agreed-upon circumstances, lessening the sense that the conversation is happening at an arbitrary time. In general, new discussions will reflect a change in the child's status, as outlined above.

This is different from the need to review and document resuscitation during each hospitalization. In fact, identifying agreed-upon times to review resuscitation, and documenting conversations when they take place, can prepare families with the necessary information at such times. Having this documentation can lessen the need for a physician unfamiliar with the child and family to pursue a lengthy discussion about resuscitation. In

addition to providing a summary of information in writing, the document can include contact information for the team most actively involved with the family. This contact can help confirm the desired medical orders and protect the family from repeating their story and decision.

Finally, again, decision making is a process. Some discussions start the process. Some help clarify a plan after experiencing an event. Others occur when the acute event has passed and a family is better rested and able to process information. The important point is recognizing that decision making is fluid, based on how the story changes and evolves. Ideally, a family has a team that will help navigate along with the story, rather than try to dictate how the story should look.

Considering resuscitation: CPR and intubation

Resuscitation involves interventions at times of respiratory failure or cardiopulmonary arrest. There are two general categories of interventions: intubation for respiratory failure and CPR for cardiopulmonary arrest. This discussion highlights the details that can be relevant when considering these interventions. The goal here is to help parents determine when they believe an intervention can provide potential benefit and when they believe an intervention should not be used, so as to avoid potential harm.

Making the "right" decision about resuscitation sometimes creates a conflict between the head and the heart. Even providing a summary of relevant details, as in the following discussion, puts the focus on the "facts" rather than on the heart. My hope and intention here is to inform families and to provide physicians with information to reflect on with families. Most important, technical details are best reviewed with a team that can provide a supportive environment and attend to the emotions that are an inevitable part of this process.

In general, the intended benefit of intubation and CPR is to extend life, if possible. The information here is framed by a consideration of the harm of these interventions and the potential benefit of limiting such interventions. The following comments are from parents of children with SNI, reflecting on why they decided to limit resuscitation.

HARM OF INTUBATION AND CPR

My son sleeps more than he used to; he is unable to enjoy his days like before. It wouldn't be fair to him to keep him around longer for me. Instead, we will focus on keeping him comfortable until his time comes.

We need to use a lot of medications to keep my daughter comfortable; she is better but not as comfortable as she deserves to be. I don't want to prolong her suffering by keeping her alive with "aggressive" interventions. We are looking to enjoy each day together, with a focus on treating her comfort, not treating the medical problems that would keep her around longer.

It wasn't until I reflected back that I realized my son used to join us in the "fight" to stay alive during each respiratory illness; now I think we are the ones fighting for him, but he seems tired of the fight.

We've noticed that the good days between each illness aren't there like they used to be; we think this is what it means to be doing "to" versus doing "for" our son.

HARM OF CPR FOR CARDIOPULMONARY ARREST

It seems like a lot to do to a body without any guarantees of success.

There is the risk of further damage to the brain when the heart stops; I can't risk putting my child through that, where he would be alive but worse off than before.

BENEFIT OF NOT USING INTUBATION OR CPR

I will be able to hold my daughter when she is dying.

Our son can be with us at home, surrounded by those who love him, when his time comes. We can't take a chance that something that might not help will take that away from us and from him.

We have noticed that my son has less benefit from each hospitalization and gets more agitated when in the hospital than he did before. It was a natural next step to not use any interventions for resuscitation, because we want to protect him from needing to go to the hospital. We would only go to the hospital if we can't keep him comfortable at home or if there is a new problem that can be "fixed."

When we made a decision to not use intubation or CPR for our daughter, we realized this also protected us against any questions if she died unexpectedly at home. We know that everyone would recognize that she was at risk for this to happen, but we would avoid the requirement that her death be reviewed.

THE MEDICAL LITERATURE indicates that 25% to 33% of all children resuscitated after cardiac arrest in the hospital survive to be discharged (Berg, Nadkarni, and Berg 2008; Topjian, Berg, and Nadkarni 2008). Some of these children have neurological injury following resuscitation, as a result of hypoxia (low oxygen level). The most common cause of cardiac arrest in children is hypoxia and an elevated carbon dioxide level (hypercarbia). These are the circumstances most relevant to children who have SNI and recurrent respiratory illness. There are no studies that look specifically at resuscitation for children who have SNI, though data on survival to discharge after cardiac arrest, as given above, probably apply.

Given that children most often have respiratory arrest rather than cardiac arrest, a child is more likely to be found with a pulse (heart beat) than is an adult. For this reason, decisions about resuscitation are initially best focused on decisions about intubation, especially for children who have SNI and recurrent respiratory exacerbations or those who have disordered central control of breathing such as central apnea.

Making decisions about intubation means making decisions about the short-term use of mechanical ventilation. When considering such decisions for a child who has SNI and recurrent respiratory illness, one family may decide to use intubation with a time-limited trial of mechanical ventilation. Another family may view using such technology as postponing the inevitable: "Even if he recovers the first time that his breathing fails, it will eventually happen again. We want to focus on all of the other things we can do, but not put him through unnecessary discomfort or the uncertainty of recovering enough to get off the ventilator."

Some families will want to take a "watch and wait" approach and make decisions "when the time comes." This is always an option, and no family should make a decision they are not ready to make. Yet it is also important to understand that such an approach, by default, is a decision to use intubation and CPR, because paramedics in the community and doctors in the hospital are required to use these interventions unless an order has been written indicating a decision not to use.

Intubation often occurs when a child who has SNI is at risk for respiratory arrest as a result of declining respiratory function (respiratory failure), rather than because of respiratory arrest. Not every child with SNI who is intubated would have died if this had not occurred. Intubation is used to prevent the potential for respiratory failure, not because the outcome is known with certainty for children who have SNI with respiratory distress. This information is not meant to minimize the significant risk

that does exist. It is based on the experience of some children surviving despite the appearance of a life-threatening respiratory illness. When intubation is part of a child's care plan, so as to provide potential benefit, the goal is to intervene sooner in order to avoid the risk of respiratory arrest. When intubation is not part of a child's care plan, so as to protect from potential harm, some children can do better than expected, given the difficulty of predicting when a significant decline in respiratory function is terminal.

There is limited information in the medical literature about the outcomes after short-term use of mechanical ventilation for respiratory failure in children who have SNI. One retrospective study reviewed the outcomes of all children with neurological impairment who were intubated and mechanically ventilated for respiratory failure (van Gestel et al. 2010). The group was divided into those who had severe impairment (children with around-the-clock care and with no ambulation or communication) and those who had moderate impairment (those with "adequate" communication and not expected to live independently). Figure 9.2 summarizes the outcomes for the 22 children who had SNI.

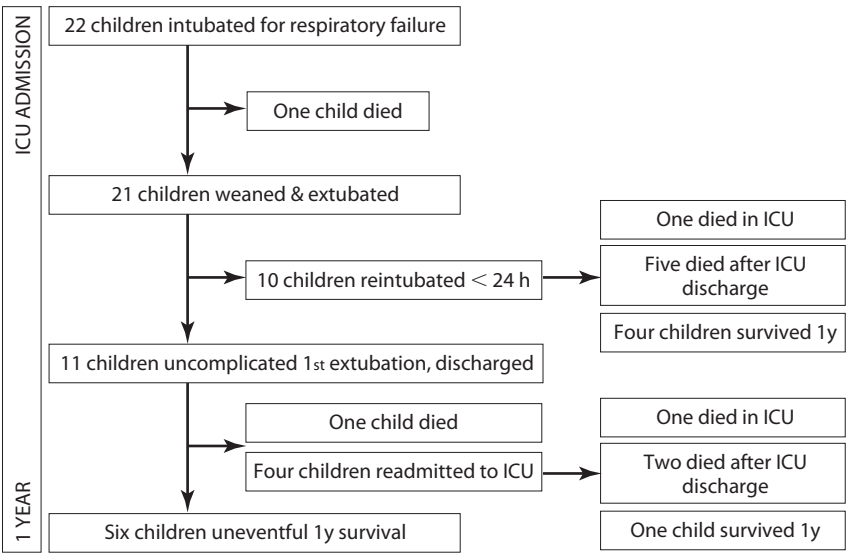

ICU ADMISSION
1 YEAR
22 children intubated for respiratory failure
One child died
21 children weaned & extubated
One died in ICU
10 children reintubated < 24 h
Five died after ICU discharge
Four children survived 1y
11 children uncomplicated 1st extubation, discharged
One child died
One died in ICU
Four children readmitted to ICU
Two died after ICU discharge
Six children uneventful 1y survival
One child survived 1y

Figure 9.2. Flow chart of intensive care unit (ICU) admission with intubation for respiratory failure in 22 children with severe neurological impairment. *Used with permission from J. P. van Gestel, A. H. Robroch, C. W. Bollen, et al., "Mechanical Ventilation for Respiratory Failure in Children with Severe Neurological Impairment: Is It Futile Medical Treatment?"* Dev. Med. Child. Neurol. *52, no. 5 (2010): 483–88, fig. 1, p. 486.*

The average duration of mechanical ventilation for these 22 children was 16 days (range 3 to 34 days). The average length of stay in the intensive care unit was 18 days (range 4 to 36 days), compared with 6 days for all children admitted to the ICU. Though the number of children in this study is small, the information indicates that children who have SNI have significantly longer hospitalizations in the ICU and require a longer time-limited trial if mechanical ventilation is attempted. We must be cautious with information from such a small number of patients, but it is useful as parents weigh decisions to "provide potential benefit" versus "avoid potential harm."

As summarized in figure 9.2, 11 (50%) of the children survived during the 1-year period of this study. Of those identified to have "chronic respiratory problems" (18 of the 22 children), 39% were alive at 1 year. Eight of the 11 deaths occurred at home, following a decision by the family not to readmit their child to the ICU, with 2 deaths occurring after a second admission to the ICU. This study concluded that the children who had SNI had repeated, prolonged, and complicated admissions to the ICU. In contrast, among the children who had moderate impairment, there were fewer deaths, reintubations, and readmissions to the ICU.

Whether this information is representative of outcomes for all children who have SNI is uncertain, given the small number of patients in the study. Of note is that the outcomes for the children who had "chronic respiratory problems" were similar to outcomes for adults with severe pulmonary disease resulting from COPD. A decision-making tool for adults with COPD indicates that, of 100 patients, 30 will come off the ventilator and survive at least 1 year, 40 will come off the ventilator and die within 1 year, and 30 will die in the hospital with the first intubation and mechanical ventilation (OHRI Patient Decision Aids 2008).

Again, these numbers must be used with caution, though they help provide a general impression. There are probably two types of respiratory problems in children who have SNI, each with a different level of risk and benefit from interventions: impaired mechanics and impaired lungs. Children with impaired mechanics are at risk for mucus plugs, atelectasis with ventilation perfusion mismatch, and pneumonia. Their condition is probably more "reversible" at times of acute decline in respiratory function than that of children with irreversible damage to the lungs. Over time, the impaired mechanics can damage the lungs. Some children might survive repeated courses of ventilation and live for long periods with chronic home ventilation before such damage occurs.

TABLE 9.5 Pros and cons of intubation/mechanical ventilation versus supportive care

	Benefit	Burden or harm
Intubation and mechanical ventilation	• May prevent immediate death • May lengthen life by a year or more • May relieve dyspnea in the short term	• Child may not be able to come off the ventilator • Underlying respiratory problems will be no better than before, and perhaps worse
Noninvasive supportive care	• Dyspnea management can be part of the long-term care plan • Care at the end of life does not involve discomfort from tubes, tests, and procedures	• May shorten life • May seem like "giving up"

When both problems exist, the outcomes might be more comparable to the data for COPD.

Table 9.5 reviews the pros and cons of hospitalization with intubation and mechanical ventilation versus noninvasive supportive care. (See table 9.8 for a review of the pros and cons of medical treatment plans that can occur in the home versus those that can occur in the hospital—another consideration that is beneficial in decision making.) As mentioned earlier, such decision making is best viewed as choosing to provide potential benefit versus choosing to avoid potential harm, rather than as "treating" versus "not treating."

Time-limited trials of mechanical ventilation

When considering the option of a time-limited trial of mechanical ventilation, families will find it useful to think about what they would anticipate doing if their child could not breathe adequately without the ventilator. Some families will know that they do not want their child to be on chronic mechanical ventilation. They may wish to use a time-limited trial, with a decision to discontinue ventilation if it is not successful after 7 to 14 days.

Other families may want to use a time-limited trial but do not want to make any decision about chronic ventilation, and instead will "cross that bridge" when necessary. To prepare, it can help to explore the feasibility of chronic home ventilation. Without some planning, a family may encounter

an outcome they had not anticipated. Questions that can be helpful here include: How many children are able to live at home with chronic ventilation in this area? How long is a child typically in the hospital until this can be arranged? How many children end up living elsewhere? These questions recognize that each community is different in terms of the resources available to support a plan of home ventilation.

As mentioned earlier, too often the focus is on the short-term plan. Thinking about long-term outcomes is also beneficial. Considering both short-term and long-term outcomes is part of the process of being informed, even before a decision needs to be made.

Decisions to discontinue mechanical ventilation

Just as it is permissible not to initiate the use of mechanical ventilation, it is permissible to stop ventilation that is not providing the intended benefit. For some families, this will occur after a time-limited trial. For others, it may occur after the child has been supported with ventilation for years. Jonathan and his family (see chapter 6) provide an example of a decision to discontinue home ventilation.

The reasons to stop a treatment are the same as the reasons not to initiate a treatment: diminishing benefit, increasing harm, or increasing suffering. When such a decision is made, a child's comfort can be maintained during the process of discontinuing this technology.

Documenting decisions

RESUSCITATION IN THE COMMUNITY

Documenting resuscitation in the community is complicated. Different states have different forms that are legally recognized by emergency medical services (EMS), and some states have no form. Forms that are legal documents in a given state include Physician Orders for Life Sustaining Treatment (POLST) and Comfort Care forms. These forms allow treatment preferences to be translated into medical orders that are recognized and honored in different care settings and by different care providers, including EMS in the community. Decision making that is typically documented in the community includes decisions about CPR, intubation, and transfer to the hospital.

The most widely recognized and used form is the Physician Orders for Life Sustaining Treatment. This form was developed in Oregon in 1991 as part of the POLST Program. It was developed to ensure that preferences

for life-sustaining treatment could be both documented and honored across different care settings, including the hospital, home, and long-term care (Hickman et al. 2005). Based on both its ease of use and its community acceptance in Oregon, POLST is now being used in other states. Information for families and for physicians can be found at the POLST website: "Paradigm," "Resources for Health Care Professionals," and "Resources for Patients & Families" (POLST 20008a, 2008b, 2008c).

Guidance is provided for healthcare professionals when using the Oregon POLST for a "person with significant physical disabilities, developmental disabilities, and/or significant mental health condition" (POLST 2011). This guidance is provided to ensure that the form is used when there is a condition that warrants completion of the form, not solely because a person has a disability. Several questions are provided to help determine whether a POLST form is warranted, including the following:

- Does the person have a disease process (not just their stable disability) that is terminal?
- Is the person experiencing a significant decline in health (such as frequent aspiration pneumonias)?
- Is the person in a palliative care or hospice program? and/or
- Has this person's level of functioning become severely impaired as a result of a *deteriorating* health condition when intervention will not significantly impact the process of decline? (POLST 2011)

Even in states where such forms are not available, steps can be taken to help ensure that decisions about resuscitation are supported in the community. Families should not feel responsible for arranging the necessary details. A primary pediatrician, social worker, palliative care team, or local hospice can navigate these details in the local community, including talking with local EMS providers and with representatives from the child's school. These conversations can help clarify how unnecessary interventions will be avoided while providing support in the moment, if needed.

In addition, families need a clear plan for how to contact members of the medical team in the moment, so as to avoid calling EMS when a crisis is occurring. Palliative care and hospice teams are a natural option, though other teams such as a complex chronic care team may be able to meet these needs. It is important to identify the team members with the skills needed and the 24/7 availability to manage concerns as they arise.

Finally, using a form to document limits to resuscitation in the community does not mean that the form must be used. Instead, the form can be

viewed as providing documentation if it is needed. This is a reminder that making a decision does not mean the decision is written in stone.

RESUSCITATION IN THE HOSPITAL

We had made the decision to not use resuscitation if our son's heart stops. When our son was later in the hospital they started asking, "Do you want us to use chest compressions, medications, or to shock your son's heart if it stops?" I was flabbergasted. It felt like we were being asked to rethink our decision and to make decisions about each intervention that can be used. After I gathered my thoughts, I explained that I had already made my decision. "I understand you have different ways to restart the heart. I don't need to know about each intervention you can use. My decision is the same here as it is when he's at home. Why do you have to treat it so differently when we're in the hospital?" I felt like such a bad mother, but I know in my heart that I'm doing the right thing.

Documentation in the hospital involves a written order indicating any limitations in the use of interventions in the event of cardiopulmonary arrest or respiratory failure. In addition to the physician's order, a note summarizing the discussion and decisions becomes part of the patient's medical record.

Community-based forms, such as POLST, document decisions about the use of intubation and CPR. Hospital-based forms often indicate each separate part of CPR, as well as other interventions that are used when respiratory problems are encountered. The interventions that might be part of a hospital-based resuscitation form, and therefore might be reviewed with a family, include the following:

- *Respiratory:* bag valve mask ventilation (bagging), intubation, mechanical ventilation, oropharyngeal (oral) airway, nasopharyngeal (nasal) airway, BiPAP or CPAP, suctioning, oxygen
- *Cardiac:* chest compressions, cardiac medications, electrical stimulation (electric cardioversion)

Parents may be asked about the different interventions that can be used; physicians may present families with a "menu" of possible interventions. It is helpful to consider respiratory failure (which can lead to respiratory arrest) separately from cardiopulmonary arrest when reviewing these interventions. This is also a time to revisit the goals of care that can help guide decisions to use intubation and CPR, and the likelihood that

use of such intervention can meet these goals. Is the primary goal to attempt a restoration of health and function to a baseline that the child currently enjoys? To minimize the use of invasive interventions while still using medical treatment options such as antibiotics? To protect from interventions that might support life yet prolong suffering?

The goal is to minimize a "check list" of options, which can confuse decisions about intubation and CPR. A trusted healthcare team can help a family think through the details and then distill goals of care into medical orders that support these goals. Families should feel in control of determining the care plan that makes best sense for their child, yet it is beneficial to minimize confusion about the interventions on the "laundry list."

As noted above, interventions that can be used acutely (in the moment) for respiratory failure and respiratory arrest include bagging, intubation, and mechanical ventilation. *Bagging* refers to the use of a bag valve mask, placed over the face to inflate the lungs when breathing is inadequate or a person is not breathing. In general, bagging serves as a bridge to artificial ventilation until intubation can occur.

Interventions that can be used to keep the upper airway open include an oropharyngeal (oral) or nasopharyngeal (nasal) airway (also known as a nasal trumpet). These interventions are most commonly used when a person is unconscious and the muscles in the jaw relax, allowing the tongue to obstruct the upper airway. The risk with an oral airway is that the gag reflex will be stimulated, resulting in vomiting.

Other interventions used to support breathing include noninvasive positive airway pressure ventilation with BiPAP or CPAP. As with invasive ventilation with a tube, decision making includes considering how these interventions will meet a child's goals of care. Some children do not tolerate this form of ventilation. In this case, adjustments of the equipment can be made, such as a change in the type of mask used, as well as considering whether the burden of the intervention is greater than the potential benefit.

Other interventions sometimes indicated on hospital-based resuscitation forms include oxygen and suctioning. As these are often used chronically for children who have SNI, they are best considered as part of a child's care plan to improve comfort.

Interventions for cardiac arrest (the heart stops) include chest compressions, cardiac shock, and medications. Children who have SNI are at increased risk for rib fractures during chest compressions, as a result of osteoporosis (because these children are nonambulatory throughout life). In addition, most children who have SNI experience cardiac arrest as a result

of respiratory failure. When breathing fails, the lack of oxygen can result in failure of the heart. When a decision is made not to intubate if there is respiratory failure, a family can be informed about the lack of benefit from CPR. When intubation remains part of the care plan, the smaller benefit from CPR, based on survival data following cardiac arrest, can be weighed against the risk of rib fractures and the risk of further injury to the brain as a result of hypoxia (low oxygen level).

Documenting "why?" in addition to "what?"

On treatment-preference forms, in addition to indicating what to do, it is beneficial to document why. A physician can provide documentation that clearly and succinctly describes the child's medical status, poor prognosis, goals of care, how the decisions support these goals, and the focus of the care plan. This can be an invaluable summary for a family. Providing such information can help others understand why certain interventions have been limited and can decrease any sense of "giving up." It can help direct other healthcare providers to the care that is appropriate and ensure that there is always care to provide.

In addition to documenting when there is a limit to interventions, it is useful to document when there is no limit. This information allows those unfamiliar with a child and family to understand that such decisions have been carefully considered. It can include information about goals of care and how the child is benefiting from the current care plan.

Two sample documents are provided below to outline how information about both types of decisions can be conveyed. In the document indicating no limit to intubation and resuscitation, a photo is included in recognition of the benefit of seeing a child at his or her best baseline. It is difficult to understand the life of a child who has SNI when the child is sick and in the hospital, and this difficulty can result in assumptions about the quality of such a child's life. Displaying and sharing photos with the medical teams in the hospital can help overcome this barrier.

Sample documents

RESTRICTION OF INTERVENTIONS

> Our team has the privilege of providing care for Carlos M. He is a 12-year-old boy who has severe neurological impairment as a result of a structural abnormality of his brain. His health is compromised, increasing the risk of a life-threatening event, including the risk of respiratory failure as a result of impaired mucus mo-

bilization, chronic aspiration of oral secretions, chronic inflammation, and intermittent infection. Other problems that increase this risk include daily seizures.

Carlos's parents have given very thoughtful consideration to their goals for their son. They wish to maximize his comfort, limit use of invasive interventions, and continue to use the noninvasive care plans that currently benefit his health. Based on these goals, a decision has been made not to attempt resuscitation (Do Not Resuscitate—DNR) and not to intubate (Do Not Intubate—DNI). These decisions also reflect the uncertainty of benefit from such interventions and the inability of such interventions to reverse or improve the underlying risk to health. They have also decided not to use CPAP or BiPAP, based on prior experience with its use. The medical team is in agreement with this plan of care for Carlos. In addition, a decision has been made to identify treatment plans that can be accomplished at home.

Carlos's respiratory illnesses will continue to be treated with antibiotics and steroids, along with other chronic interventions such as suctioning, oxygen as needed, and chest PT. In addition, morphine sulfate will be used as needed for respiratory distress. This has been used previously with benefit during an acute respiratory illness.

Hospitalization will be reserved for new, potentially reversible problems, such as a bone fracture. Other considerations include persistent discomfort and distress that is not being adequately managed at home. If Carlos is hospitalized, the goal is to avoid invasive interventions and only to consider such interventions if it is certain that a problem can be reversed and allow recovery. Restrictions in interventions include do no attempt resuscitation and do not intubate.

The state-recognized Physician Orders for Life Sustaining Treatment form has been completed. [Alternatively, if the state does not have an out-of-hospital resuscitation order form, the family would contact the team if there were urgent questions or concerns at home, with a goal to minimize unintended calls for EMS.]

Our team remains available at [phone number] to assist with any part of Carlos's care plan.

NO RESTRICTION OF INTUBATION

Our team has the privilege of providing care for Carlos M. He is a 12-year-old boy who has severe neurological impairment as a result of a structural abnormality of his brain. His health is compromised, increasing the risk of a life-threatening event, including the risk of respiratory failure as a result of impaired mucus mobilization, chronic aspiration of oral secretions, chronic inflammation, and intermittent infection. Other problems that increase this risk include daily seizures.

Carlos's parents have given very thoughtful consideration to their goals for their son. Though Carlos has experienced increasing frequency of respiratory illnesses, he continues to return to his prior baseline following treatment for

each illness. He is typically admitted to the hospital for each respiratory illness, currently every 4 to 6 months. In between illnesses, Carlos is able to participate in his daily activities through school and with family. Information that indicates his enjoyment in these activities includes his ready smile and consistent response to the things he enjoys most. Included with this document is a recent photo that represents Carlos when he is well. Parents wish others to understand how well he is thriving between each illness. They recognize that this is not evident when he is sick and in the hospital.

In the event of respiratory failure, parents request that Carlos be intubated and supported with mechanical ventilation. They recognize that some children do not fully recover the ability to breathe without mechanical support. They do not wish to anticipate what their decision will be if that were to occur. These decisions are shared and supported by Carlos's medical team.

Parents do not want interventions to restart the heart (no chest compressions, no cardiac shock, no cardiac medications) if there is cardiopulmonary arrest. They recognize that this will be documented as Do Not Resuscitate (DNR). This decision is based on the goal of protecting Carlos from the risk of rib fractures and the risk of further injury to the brain as a result of hypoxia. They believe that Carlos has a higher likelihood of benefit from intubation when his breathing is failing and a lower likelihood of benefit if his respiratory problems progress to cardiopulmonary arrest.

Parents have identified the following goals as an ongoing guide to decisions: they wish to use medical treatments that give Carlos a "reasonable" chance of recovery, they will continue to focus on how Carlos is able to enjoy each day, and they will revisit their decisions if there is a decline in this enjoyment or if they believe that he is suffering.

The state-recognized Physician Orders for Life Sustaining Treatment form has been completed to indicate "Intubate and/or Ventilate," "Do Not Resuscitate," and "Transfer to Hospital." [Alternatively, if the state does not have an out-of-hospital resuscitation order form, the family would contact the team if there were urgent questions or concerns at home.

Parents understand that during each hospitalization they will be asked about their preference for intubation and resuscitation. They hope that this document will serve to help those who do not know Carlos understand and respect the decisions, which they have given careful consideration to. If there is a significant change in Carlos's health and there are decisions to consider, they request that a member of our team be present for any discussions about his care plan. Our team remains available at [phone number] to assist with any part of Carlos's care.

Beyond resuscitation: reviewing other parts of the care plan

It was time for her suffering to stop and for my suffering to begin.

Unlike decisions about resuscitation, other parts of the medical treatment plan can feel like "routine" interventions, necessary to continue. In addition, such medical treatment is often used for many years with benefit. It can feel disorienting to consider that something that is routine and has provided benefit for a long time could now be the cause of problems.

The American Academy of Pediatrics (AAP) policy statement on forgoing medical treatment recognizes the range of such treatment: "Life-sustaining medical treatment [LSMT] encompasses all interventions that may prolong the life of patients. Although LSMT includes the dramatic measures of contemporary practice such as organ transplantation, respirators, kidney (dialysis) machines, and vasoactive drugs, it also includes less technically demanding measures such as antibiotics, insulin, chemotherapy, and nutrition and hydration provided intravenously or by tube" (AAP 1994). Examples of "less technically demanding" LSMT for children who have SNI are treatment during acute respiratory exacerbations with antibiotics, prednisone, and chest PT or a pulmonary vest; use of steroids for a patient with glucocorticoid deficiency, including daily and stress doses; use of a bag valve mask (Ambu bag) for a child with a tracheostomy, to intermittently inflate the lungs; and use of medical fluid and nutrition, provided by a feeding tube.

The goal in reviewing a child's care plan is to ensure that medical interventions are used when beneficial and discontinued when they have no benefit or cause more harm than benefit. Medications can be reviewed to determine whether any would have no ongoing benefit as goals have shifted or at the end of life. Examples include supplements such as multivitamins and carnitine; promotility medications, as the feeding volume is decreased or stopped; and chronic respiratory treatments, such as montelukast (Singulair) and inhaled steroids.

If there is ongoing harm from an intervention, then consideration can be given to forgoing that treatment. As an example, one family decided to stop using antibiotics for respiratory exacerbations, because their daughter had developed severe diarrhea as a result of recurrent *Clostridium difficile* that was difficult to treat and a source of significant problems. Other examples reflect a decline in benefit or an increase in suffering that is prolonged by the ongoing use of medical treatment that can prolong life. For one family, a decline in their son's alertness resulted in decisions not to treat respiratory exacerbations with antibiotics, steroids, and chest PT and instead to focus on the use of treatment to promote comfort. For another family, the same decision was based on their child's increased suffering with each respiratory exacerbation, with episodes becoming more

frequent and prolonged. One family summarized their journey thus: "When did we go from *assisting* our son with his breathing to *insisting* that he breathe?" (Duncan 2011).

This is also a time to review the role of monitoring, such as the use of a pulse oximeter. Questions that can help guide decisions to discontinue monitoring include: What will we do with the information? Are we using this more for our peace of mind? Is it taking our focus away from our daughter? It can initially be distressing to give up the "safety net" of the information from monitoring, then can later be liberating as unnecessary "noise" that will not change the care plan is removed.

Comfort at the end of life: the role of planning

A peaceful death takes planning. It requires stepping back from the medical model of testing, monitoring, and treating when such endeavors have decreasing benefit for a child. Planning for comfort at the end of life is not about "giving up" but about protecting from potential harm. Children who have SNI are vulnerable to complications and discomfort from the continued use of medical interventions at the end of life. They are especially vulnerable because of the difficulty in recognizing when someone with a chronic condition is "failing" and dying.

Increasing the use of treatment interventions as health continues to decline only increases the harm from such interventions. There is no definite "marker" to indicate when the "line" has been crossed, yet recognizing the benefit of a "natural death" can assist with decisions along the way. This information is intended to help when considering the benefit and harm of treatment decisions.

Because children who have SNI often experience decline over a long time, the likelihood of "aggressive" evaluation and treatment at the end of life is increased. Rather than focusing on defining the "line" in such children, it can help to consider what happens as the body is slowing down as the result of an ongoing decline in health or further changes in the CNS. This is a time when chronic and acute treatments have declining or limited benefit for the health of the body. It helps to ask: What interventions might be discontinued that once were beneficial but now are causing harm or have no ongoing benefit? When is a new intervention more likely to not help, cause harm, or prolong suffering? These considerations can help minimize unintentional harm from the treatments routinely used for children who have SNI.

An important consideration for these children is complications from tube feedings as health continues to deteriorate. As health is declining, the blood vessels can become "leaky," causing fluid to enter the tissue spaces of the body, including the skin (resulting in edema) and the lungs (pulmonary edema). As the body is slowing down at the end of life, there is a decline in the motility of the intestines and the function of the kidneys. When someone is receiving medical fluids and nutrition through a feeding tube or an IV line at such times, this can result in vomiting, retching, discomfort with feedings, increased respiratory secretions, and extra fluid in the skin causing puffiness (edema). These changes can contribute to discomfort. Vomiting and fluid in the lungs can worsen breathing and cause respiratory distress. This is a time to balance a search for reversible causes with a consideration of irreversible decline.

It can help at such times to approach a change in the care plan as a temporary "trial." This is similar to an empirical medication trial for a potential source of pain, such as central neuropathic pain; benefit from a medication directed at the problem is indirect evidence of this source of pain. In the same manner, discontinuing a treatment previously used can be approached as an empirical trial, with the option to restart the treatment. Nothing will be lost from such a trial, and information will be gained.

This approach is illustrated by the case of Grace, at the end of chapter 6. She had significant improvement in symptoms when her tube feedings were decreased by 35%. This benefit continued for 4 weeks. When symptoms returned and were more severe, she had dramatic improvement in comfort when all medical fluids were stopped. Her parents wished to see whether the problem was temporary, so a minimal volume of fluid was tried 2 days later. Each time, the plan was adjusted based on its effect on Grace and the ability of the plan to maintain her goal of comfort. This process recognized that the change in Grace's condition might be an irreversible change, with greater harm than benefit from the continued use of tube feedings and fluid. The following directive supports these considerations: "Medically assisted nutrition and hydration become morally optional when they cannot reasonably be expected to prolong life or when they would be 'excessively burdensome for the patient or [would] cause significant physical discomfort'" (United States Conference of Catholic Bishops 2009).

When symptoms suggest a significant slowing of the intestines as health is declining, it can help to give an amount by feeding tube that is tolerated, rather than focusing on a "required" amount. Sometimes this will be a temporary change during an acute illness, with a return to

former feeding volumes when health improves. It can include the option of switching from formula to an electrolyte solution during the first 24 hours of a significant illness, which can decrease the risk of vomiting. At other times, the inability of the body to tolerate feedings can be an indication of a serious decline in health or an irreversible change in the CNS. This is not an "absolute" marker, but it suggests the benefit of reconsidering what is "required" to be given by feeding tube. The problems that can occur with artificial fluids and nutrition often lessen when the amount given is decreased.

The risk and associated distress of overfeeding at such times is much greater than that of a trial using 30% to 50% less than was previously received. Yet it is naturally distressing to "undo" years of thinking in terms of what is "needed." For some children, this situation reflects a decline in metabolic needs as the child becomes less active. It is not uncommon for children who have SNI to live for months or longer while receiving significantly fewer calories and fluid than they would be expected to require. For other children, the function of the intestines deteriorates when there is a change in the area of the CNS involved in the autonomic regulation of intestinal motility. In addition, edema can develop and worsen as health irreversibly declines. For children in these situations, improvement in comfort and feeding tolerance and decrease in edema help define the amount to give.

The thought of stopping medical fluids and nutrition, as was done for Grace, can cause worry that the child will starve or suffer from dehydration. There are changes in the body at the end of life that prevent a person from experiencing any hunger or discomfort as the body becomes unable to process nutrition and fluids. It is a natural process that promotes comfort; artificial fluids at this time can cause more harm than good.

This is a time to have a supportive team to assist with such decisions. The information provided here is intended to highlight the benefit of shifting from "treatment" to a "natural" approach to care. This shift from the "artificial" approach of treatment can lessen unintended harm. Parents may notice a brief period of improved comfort and interaction, at times lasting for days to weeks, occasionally for months, when a shift away from "artificial" treatment occurs. This topic is covered in more detail in chapter 10.

Eva is a 19-year-old who has SNI with a history of recurrent respiratory illness. Her chronic treatment includes an inhaled steroid, albuterol and ipratropium nebs, montelukast, daily chest PT, and BiPAP at night. The frequency of respiratory exacerbations has increased, previously occurring every 2 to 4 months for several years, now monthly over the past 4 months. Features include an increase

in respiratory rate and secretions, a decrease in oxygen saturation (O_2 sats), and working harder to breath. Each exacerbation is treated with an antibiotic and prednisone by G tube, with prednisone tapered over 2 weeks, as well as inhaled tobramycin for 2 weeks each month for the past 4 months. Prior decisions include do not attempt resuscitation and do not intubate.

There is significantly less recovery following treatment for each exacerbation. Eva's mother notes, "She is not bouncing back to her baseline like she has before and not able to enjoy her days as much." A decision is made to treat one last time with antibiotics (including inhaled tobramycin) and prednisone, with her parents anticipating limited benefit.

Eva's family and caregivers observe severe respiratory distress during each illness. They are fearful about treating this distress with morphine yet are concerned about her suffering. Her parents feel they understand the "facts" about the safety of morphine, yet they worry that they may lose Eva if morphine is used. A lower starting dose is offered, with the plan to increase the dose by 50% if there is no benefit. The initial dose provides benefit, noted as Eva looking more relaxed, with a decrease in her respiratory rate and heart rate, and with no change in her O_2 sats. Three weeks later, the morphine dose is increased by 50% and scheduled around the clock, to treat distress that is now occurring daily. The prn dose is available as often as every hour. Her comfort improves significantly. One week later her fluids are decreased by 30% because of persistent edema in her hands and feet, and sounding "wet" rather than her typical congestion. At this time, continuous pulse oximeter monitoring is discontinued. One week later there is a significant increase in dyspnea and agitation. The morphine dose is increased several times, a total increase of 130%, with prn lorazepam added to her care plan. In addition, her fluids are decreased by 15%, and less essential medications are discontinued.

Over the next 4 weeks, Eva is described as "the best she has looked in 6 months." Her O_2 sats has remained stable when checked occasionally. Her parents are struck that the benefit seen in Eva has come from the addition of symptom treatment, given that the last treatment course with antibiotics and prednisone was completed 7 weeks ago. Her parents wonder whether she would have died sooner without symptom treatment: "She was working so hard to breathe. Continued stress like that can't be good for the body." They are prepared for ongoing adjustments to Eva's care plan, such as increasing the morphine dose by 50% to 100%, decreasing fluids, and stopping feeds as needed. They are delighted that Eva can be both comfortable and awake, currently enjoying her days. They hope for as many good days as possible, yet feel prepared for the time when the primary goal will be her comfort at the end of her life.

DECISION MAKING is a fluid process, based on how the child's story changes and evolves. Some discussions start the process. Some experiences help clarify a plan.

Medical decision making for children who have SNI is often a balance between using medical interventions that can enhance a child's life and limiting their use when they make a child's life increasingly dependent, beyond a threshold that a parent views as beneficial. This book attempts to increase an understanding of the available options and to provide a balanced approach to considering these options. It is naturally easier to talk about why something should be done than about why it might not make sense to do something.

There is no wrong decision, though there are poorly informed decisions. The hope here is that parents and physicians can work together, with expert facilitation and support when needed.

TAKE-HOME POINTS

- The goal of decision making is to integrate factual information with the goals, beliefs, and values of a family.
- It is helpful to consider the various parts that can factor into decision making:
  - *Consideration of all options:* This is a process of considering the known risks and benefits of each option, including the risks and benefits of not using an intervention.
  - *Evidence for each option:* Evidence for most options used for children who have SNI indicates that the interventions can be considered but should not be viewed as needed or required.
  - *Timeline and time-limited trials:* A timeline for deciding about a surgical intervention can be identified; in addition, a time-limited trial can be considered for interventions such as mechanical ventilation.
  - *Minimizing the bias of language:* When the outcome is uncertain, it is helpful to consider a decision to use an intervention as a decision to "provide potential benefit" and a decision not to use an intervention as a decision to "avoid potential harm."
  - *A child's health trajectory:* Reflecting on a child's past allows a review of how a child is benefiting from a treatment today, including any decline in health (none, a little, a lot), as well as comfort and the ability to enjoy each day.

  - — *Goals of care:* Common goals include to maximize comfort, slow the decline in health, restore health during acute respiratory illnesses, minimize the use of invasive interventions, maximize time together as a family, maintain care at home, and avoid future hospitalizations (how these goals are prioritized can change over time).
  - — *Attention to symptom treatment:* By increasing an awareness of the benefit and safety of symptom treatment, the fear that a child will suffer without an intervention, such as intubation, can be minimized.
  - — *A team of experts for psychosocial needs:* Social workers, child life specialists, chaplains, and others can assist with practical care needs, as well as with the stress of decision making; palliative care teams include such experts.
  - — *Preferred location of care at the end of life:* The family and the team can discuss decisions and plans to help support a preference.
  - — *Worries:* A team that includes social workers, child life specialists, and others can assist with families' worries about how this experience might affect siblings, worries about finances, considerations of long-term outcome, and other concerns.
  - — *Feasibility:* A team can also review the resources that exist in a community to support a specific decision.
- Decision making can be supported by a team of experts, including physicians, social workers, child life specialists, nurses, and chaplains.
- Types of decisions to consider include those in table 9.6.
- Families need to make time to consider information. Finding time can be challenging, yet making the time to review and consider information can be invaluable.
- There are times to consider reviewing intubation and resuscitation:
  - — When there is a potential risk for a life-threatening event
  - — When there are indicators of decreasing benefit from the chronic care plan, as indicated by frequency of acute illness, frequency of hospitalization, decrease in ability to enjoy each day, and increase in physical suffering
- The risk of a life-threatening event increases in some circumstances:
  - — Severe compromise to breathing, indicated by no gag reflex or cough, severe hypotonia, and disordered central control of breathing

TABLE 9.6 Decisions to consider

Decision type	Comments
Surgical decisions	• Identified as interventions for specific problems • Decisions that can be anticipated and considered, often over several months
Intubation; cardiopulmonary resuscitation (CPR)	• Interventions for potentially life-threatening events • Decisions that are avoided if not anticipated • Decisions that often, though not always, can be anticipated, allowing time for consideration
Reviewing other parts of the care plan when the goals of care have changed	• Often, decisions to discontinue a part of the care plan that is contributing to suffering or not providing benefit
Location of care	• Considering the pros and cons of hospital care versus home-based care, especially when there is decreasing benefit or increasing distress from hospitalizations

  - — Increasing need for chronic respiratory treatments, increasing frequency of respiratory illnesses, and decreasing benefit from acute treatment for each illness
  - — Increasing frequency of hospitalizations
  - — Risk for sudden, unexpected death associated with conditions that result in disordered breathing with central hypoventilation and apnea
- A family should make a decision about an intervention once they have enough information to make that decision; they should not feel rushed.
  - — Surgical interventions:
    - The decision can often be considered over several months.
    - A timeline can be identified by the medical team and surgeon.
  - — Intubation and resuscitation:
    - Some families feel comfortable making a decision before a life-threatening event occurs, including the decision to use (provide potential benefit) or to limit (avoid potential harm) these interventions.
    - Some families will not be ready to make a decision either way. No decision should feel rushed. In this circumstance, intubation and CPR will be attempted if there is a life-threatening

event, because they are required unless an order exists to limit their use. Some families need more information, more time, or the direct experience when a child has a potentially life-threatening event.

- Specific decisions are required for the following:
  - *Surgical intervention:* See table 9.4 and information in relevant chapters.
  - *Resuscitation:* CPR is used when a child's breathing and heart have stopped (table 9.7). It is an attempt to restart the heart and to support breathing. It is often not successful. This intervention involves
    - inflating the lungs with a mask over the face or a tube inserted into the windpipe;
    - repeatedly pushing down very firmly on the chest, referred to as cardiac compressions, to mimic the heart's function and cause blood to circulate;
    - using electric shocks in an attempt to correct the rhythm of the heart or to restart the heart, referred to as electrical cardioversion (cardiac shock); and/or
    - using drugs in an attempt to correct the rhythm of the heart or to restart the heart.
  - *Intubation:* This intervention involves inserting a tube into the windpipe (trachea). It is used when a child has declining respiratory function (respiratory failure) that places the child at risk for respiratory arrest (table 9.7).
  - *Location of care:* Hospitalization can be beneficial for many problems; for some children, the benefit can lessen over time. The associated distress of hospitalization becomes more burdensome when a child has chronic, irreversible problems (table 9.8).
- Any limitation of care in one area will not alter care in other areas.
- Team members can assist with the necessary documentation about resuscitation, both in the hospital and in the home.
- Goals of care can shift from disease-modifying to providing comfort; such shifts can then guide decisions about intubation, resuscitation, and location of care.
- A goal for comfort at the end of life requires planning.

TABLE 9.7 Considering the benefits and burdens of CPR and intubation

Benefits	Risks or burden
CPR	
May restore the function of the heart: studies show that 25% to 33% of all children who were resuscitated for cardiac arrest in the hospital survived to be discharged	• Risk of rib fractures from chest compressions • Risk of further brain injury due to hypoxia (decreased oxygen to the brain) • Parents unable to hold their child at the end of life
Intubation/ventilation	
May lengthen life by a year or more: in one study of 22 children with SNI, 50% were alive at 1 year (39% of the children indicated to have "chronic pulmonary problems"); six (27%) of the children alive at 1 year had an event-free 1-year survival, with no reintubation in the ICU and no further hospitalizations	• May not be able to come off the ventilator • Underlying respiratory problems no better than before, and perhaps worse

TABLE 9.8 Considering the benefits and burdens of home versus hospital

	Benefit	Burden or harm
Home	• Earlier initiation of acute treatment with home protocols (see figure 6.4) • Avoids invasive testing and IV placement • Familiar setting for child • Less disruptive	• Caregiver fatigue • "I'm not a doctor" • "Could we have done more?" • Challenge of identifying respiratory decline that may result in respiratory failure (for children with no restrictions on resuscitation)
Hospital	• More frequent airway clearance • Allows monitoring for respiratory failure (when the plan includes use of mechanical ventilation if needed) • IV antibiotic options for broader coverage • Short-term use of noninvasive ventilation (CPAP, BiPAP)	• Disruptive • Family feeling not in "control" of care plans; their expertise sometimes dismissed • Frequent use of invasive tests and procedures (blood tests, IV placement, etc.) • Infection by antibiotic-resistant bacteria, hospital-acquired and a result of broad-spectrum IV antibiotic use

References

AAP (American Academy of Pediatrics) Committee on Bioethics. 1994. Guidelines on forgoing life-sustaining medical treatment. *Pediatrics* 93(3):532–36.

Berg MD, Nadkarni VM, Berg RA. 2008. Cardiopulmonary resuscitation in children. *Curr Opin Crit Care* 14(3):254–60.

Curtis JR, Engelberg R, Young JP, et al. 2008. An approach to understanding the interaction of hope and desire for explicit prognostic information among individuals with severe chronic obstructive pulmonary disease or advanced cancer. *J Palliat Med* 11(4): 610–20.

DiMaggio C, Sun LS, Li G. 2011. Early childhood exposure to anesthesia and risk of developmental and behavioral disorders in a sibling birth cohort. *Anesth Analg* 113(5): 1143–51.

Duncan J. 2011. Letter to the author. Mar. 20.

Dussel V, Kreicbergs U, Hilden JM, et al. 2009. Looking beyond where children die: determinants and effects of planning a child's location of death. *J Pain Symptom Manage* 37(1):33–43.

Feudtner C. 2007. Collaborative communication in pediatric palliative care: a foundation for problem-solving and decision-making. *Pediatr Clin North Am* 54(5):583–607, ix.

Feudtner C. 2011. Partnering leadership. *Arch Pediatr Adolesc Med* 165(6):487–88.

Feudtner C, DiGiuseppe DL, Neff JM. 2003. Hospital care for children and young adults in the last year of life: a population-based study. *BMC Med* 1:3.

Feudtner C, Hexem K, Rourke MT. 2011. Epidemiology and the care of children with complex conditions. In *Textbook of Interdisciplinary Pediatric Palliative Care*, ed. Wolfe J, Hinds PS, Sourkes BM, pp. 8–14. Philadelphia: Elsevier Saunders.

Flick RP, Katusic SK, Colligan RC, et al. 2011. Cognitive and behavioral outcomes after early exposure to anesthesia and surgery. *Pediatrics* 128(5):e1053–61.

Goulet O, Jobert-Giraud A, Michel JL, et al. 1999. Chronic intestinal pseudo-obstruction syndrome in pediatric patients. *Eur J Pediatr Surg* 9(2):83–89.

Heneyke S, Smith VV, Spitz L, Milla PJ. 1999. Chronic intestinal pseudo-obstruction: treatment and long term follow up of 44 patients. *Arch Dis Child* 81(1):21–27.

Hexem KR, Bosk AM, Feudtner C. 2011. The dynamic system of parental work of care for children with special health care needs: a conceptual model to guide quality improvement efforts. *BMC Pediatr* 11:95.

Hickman SE, Hammes BJ, Moss AH, Tolle SW. 2005. Hope for the future: achieving the original intent of advance directives. *Hastings Cent Rep* 35(6 Suppl):S26–30.

Holloway RG, Quill TE. 2010. Treatment decisions after brain injury—tensions among quality, preference, and cost. *N Engl J Med* 362(19):1757–59.

Jancar J, Speller CJ. 1994. Fatal intestinal obstruction in the mentally handicapped. *J Intellect Disabil Res* 38(Pt 4):413–22.

Kreichergs UC, Lannen P, Onelov E, Wolfe J. 2007. Parental grief after losing a child to cancer: impact of professional and social support on long-term outcomes. *J Clin Oncol* 25:3307–12.

OHRI (Ottawa Hospital Research Institute) Patient Decision Aids. 2008. Making choices: the use of intubation and mechanical ventilation for severe chronic obstructive pulmonary disease (COPD). http://decisionaid.ohri.ca/docs/das/COPD.pdf.

POLST. 2008a. Paradigm. www.ohsu.edu/polst/index.htm.

POLST. 2008b. Resources for health care professionals Oregon. www.ohsu.edu/polst/programs/OregonHealthCareProfessionals.htm.

POLST. 2008c Resources for patients & families Oregon. www.ohsu.edu/polst/programs/OregonPatient.htm.

POLST. 2011. Guidance for Oregon's health care professionals. www.ohsu.edu/polst/programs/documents/Guidebook2011V2.pdf, pp. 17–19.

Quill TE, Holloway R. 2011. Time-limited trials near the end of life. *JAMA* 306(13):1483–84.

Salzburg Global Seminar. 2011. Salzburg statement on shared decision making. *BMJ* 342: d1745.

Tamburro RF, Shaffer ML, Hahnlen NC, et al. 2011. Care goals and decisions for children referred to a pediatric palliative care program. *J Palliat Med* 14(5):607–13.

Topjian AA, Berg RA, Nadkarni VM. 2008. Pediatric cardiopulmonary resuscitation: advances in science, techniques, and outcomes. *Pediatrics* 122(5):1086–98.

United States Conference of Catholic Bishops. 2009. *Ethical and Religious Directives for Catholic Health Care Services*. 5th ed. www.usccb.org/about/doctrine/ethical-and-religious-directives, pp. 21, 31.

Valencia FG. 2010. Management of hip deformities in cerebral palsy. *Orthop Clin North Am* 41(4):549–59.

van Gestel JP, Robroch AH, Bollen CW, et al. 2010. Mechanical ventilation for respiratory failure in children with severe neurological impairment: is it futile medical treatment? *Dev Med Child Neurol* 52(5):483–48.

Williams RK. 2011. The pediatrician and anesthesia neurotoxicity. *Pediatrics* 128(5):e1268–70.

CHAPTER 10

Care at the End of Life

Death had indeed come slowly, but then arrived too fast.
—Chris Feudtner

Excellent care at the end of life is every bit as important as the care provided throughout life. In fact, end-of-life care is, ideally, a continuation of the best care that medicine has to offer to children who have severe neurological impairment and their families. The preceding chapters have highlighted this continuum by reviewing areas of care need and approaches to decision making, including how the goals of care can change from disease-modifying treatment to care plans that focus on improving comfort.

No parent can truly be ready to think about and prepare for the death of a beloved child. As with other chapters, this chapter is not advocating a need to accept the inevitable. Instead, it provides information for understanding and consideration that can be consulted whenever it may be helpful and whenever it is needed. Preparing for death can be tremendously difficult, yet families often describe gaining a sense of relief with planning, of feeling less burdened, as if a significant weight has been lifted from their shoulders. Preparing often includes the following:

- Identifying the members of the care team
- Making memories
- Considering the preferred location of death (home, hospital, or hospice, for example)
- Documentation
- Funeral planning
- Considering autopsy, including the Brain and Tissue Bank
- Anticipating symptom management needs when comfort becomes the primary goal of care
- Anticipating physical changes at the end of life

A TEAM TO ATTEND TO THE NEEDS OF THE CHILD AND THE FAMILY

The emotional distress of thinking about or planning for a child's end-of-life care sometimes creates a barrier to the planning that can, in fact, decrease such distress. This is a time to seek out support from experts, such as social workers, child life specialists, and chaplains. Table 9.2 summarizes how different experts can support the needs of the child and the family.

In some communities, a team can be drawn from pediatric palliative care and hospice. In communities without pediatric teams, adult hospice teams can often work directly with a child's pediatric physicians. Though an adult hospice may have limited experience with the care of children, they have expertise in end-of-life care. For some families, end-of-life care may involve the creation of a "virtual" team, which is available from a distance as a resource for the local, "on site" team in the community.

These teams can help lessen the burden for families by overseeing or helping with details, including documentation, communication with emergency medical services (EMS), and funeral planning. Such assistance can help families complete tasks, which can then be put aside so that a family's focus can remain on their child.

MAKING MEMORIES

Part of preparing includes reflecting on a child's life. Many families talk about the "gift" that their child has brought to their life, in ways that no one could imagine. Preparing for a child's end of life is a time to reflect on that child's story. Siblings can be part of this process. Child life specialists can help with this process for siblings and provide tools to honor the legacy of a child's life.

LOCATION OF DEATH

Planning the location of death has a significant impact on where the death of a child will occur. In one study, when parents planned, the majority of children died at home (Dussel et al. 2009). In contrast, when no planning took place, the majority of children died in the hospital. Parents who had an opportunity to plan were significantly more likely to be very comfortable with the location of death and less likely to have preferred a different location.

This planning requires a team to assist with the details. Social workers can identify community resources, child life specialists can support and involve siblings in the process, and the medical team can anticipate the needed care plan. In addition, families need a clear plan on how to contact members of the team when they are needed, so that a family can avoid calling EMS when a crisis occurs. Everyone involved should know which experts are available 24/7 to manage concerns as they arise.

DOCUMENTATION

Documentation is the process of translating treatment preferences into medical orders. The team assisting with details can provide the appropriate forms, assist with the documentation, and communicate plans to others, as needed. The forms and details of documentation are reviewed in chapter 9.

FUNERAL PLANNING

Funeral planning is, understandably, a distressing process even to think about, because it reflects an "acceptance" of what is to come. There is no right time to complete this task, but starting it earlier can save effort later, when planning may be more difficult. Many families view this planning as the hardest thing they ever had to do, but once it was done, it gave them tremendous peace of mind.

There are two components to consider: identifying the funeral home, and deciding how to honor the child's life. A social worker, pastor, or friend can assist, as can child life specialists, who can help involve siblings on a level that is appropriate and comfortable.

Some families start this planning when the goals of care have shifted from disease-modifying care to comfort, rather than waiting until death is "certain." For some, planning will have occurred months before the child dies. Identifying this task for families earlier allows them to feel that planning takes place "on our time."

AUTOPSY AND THE BRAIN AND TISSUE BANK

An autopsy is an examination of a body, including the organs of the body, following death. It answers questions about a child's death and advances knowledge about a disease. The option of an autopsy is best discussed with a trusted physician before the child's death, which gives

families time to consider the information. The reason autopsy is included in the list of tasks in this chapter is to make sure that families are fully informed, to help avoid regrets later.

It is natural for a family to decline autopsy. They may feel that their child has "been through enough." After having time to consider, many families do choose not to pursue an autopsy, but others consider an autopsy to be an opportunity to answer lingering questions that are causing distress. Still other families feel that it is a way to advance science and help other children. If an autopsy is completed, parents can arrange to review the reported results with their child's physician at a time when they are ready.

A specific type of autopsy can be arranged with the National Institute of Child Health and Human Development (NICHD) Brain and Tissue Bank. The goal of the bank is to advance scientific research on developmental disorders. It serves the critical purpose of collecting, preserving, and distributing human tissues to qualified scientific investigators who are dedicated to the improved understanding, care, and treatment of children who have developmental disorders, offering hope to others.

In deciding whether to donate to the NICHD Brain and Tissue Bank, the following points are helpful:

- The procedure to recover tissue at the time of death will not interfere with open casket viewing.
- Tissue and organ donation is acceptable to most major religious organizations.
- The Brain and Tissue Bank covers extra expenses related to the recovery of tissue. No financial burden is placed on the family as a result of this decision to donate tissues.
- All donor information remains anonymous, and anyone who registers with the bank holds the right to withdraw at any time. Further information for families is available at www.btbankfamily.org.

WHEN COMFORT BECOMES THE PRIMARY GOAL OF CARE

Symptoms that may require management at the end of life for children who have SNI include pain, agitation, increased movement, seizures, vomiting, feeding intolerance, respiratory distress, and secretions. Symptom treatment plans for these potential problems can be developed in advance. The principles of symptom management reviewed in chapter 4 remain

relevant throughout the child's life, including the use of medications and nonpharmacological strategies. Some sources of discomfort in a child can be addressed by reviewing and stopping any treatment that can contribute to distressing symptoms.

Reviewing the end-of-life symptoms that sometimes occur in children who have SNI can increase parents' worry that their child will suffer at the end of life. The goal of this section is to help prepare medical teams with the necessary information to ensure that, if a distressing symptom *does* occur, there is a treatment plan that can be initiated. With knowledge and planning, any discomfort that arises at the end of life in children who have SNI can be managed.

Pain and agitation

When there is an escalation in agitation at the end of life, pain must be considered as a possible cause. Other causes include paradoxical reactions to benzodiazepines and anticholinergics, medication withdrawal, or akathisia (an unpleasant sensation of inner restlessness) resulting from antipsychotics. In addition, a significant increase in the dose of an opioid can sometimes result in agitation due to hyperalgesia. In general, when agitation worsens despite the start or increase in dose of a medication, it is helpful to review potential contributing causes such as undertreated pain or an unwanted effect from a medication.

Seizures

Seizures may result from progression of the underlying disease or from an inability to absorb an antiepileptic medication due to progressive slowing of intestinal motility. If an antiepileptic drug (AED) is not tolerated by feeding tube, some AEDs can be given rectally, including phenobarbital, carbamazepine, lamotrigine, and valproic acid (Birnbaum et al. 2001; Epilepsy.com 2011; Graves et al. 1989; Smith, Sharkey, and Campbell 2001).

Small, self-limited seizures that do not cause distress may not need treatment. If needed, treatment options include phenobarbital, which can be given rectally if necessary and has the added potential benefit of treating associated agitation at the end of life (Cheng, Roemer-Becuwe, and Pereira 2002; Stirling, Kurowska, and Tookman 1999). Breakthrough seizures can be treated with buccal or rectal benzodiazepines, as discussed in chapter 7. Some children may benefit from a scheduled or continuous

benzodiazepine. Attention to overall pain and symptom management is an essential part of seizure management at the end of life.

Medications

Managing symptoms at the end of life involves many of the medications reviewed in earlier chapters. One primary difference may be the route of delivery. If the motility of the gastrointestinal tract slows down, giving medications by a feeding tube may become more difficult or less effective. In this case, it is helpful to consider medications that can be given by mouth (sublingually or buccally) or rectally. Pediatric palliative care and hospice teams can give assistance and guidance by providing direct care or by providing guidance in consultation with a child's local physician.

Pain and agitation have similar features and are helpful to consider together. Also, as noted above, pain can be a source of agitation. An increase in muscle spasms, stiffening, and arching may accompany pain and agitation, or may indicate progressive changes in the central nervous system if there is further loss of inhibition and/or increase in excitation in the CNS. Keeping these processes in mind can help providers decide what medications to consider if a child has an increase in any of these features. Medication options are summarized in table 10.1.

Selection of medication for agitation/pain at the end of life will be empirical. It can be helpful to consider a medication from a second category if symptoms have not improved with medication from a first-used category. There are no hard-and-fast rules. Sometimes the combination of two

TABLE 10.1 Pharmacological treatment of symptoms at the end of life

Medication	Problem to treat	Comments
Opioids	Pain, dyspnea	• Opioids such as morphine can be given sublingually, using the concentrated form
Benzodiazepines	Agitation, seizures	• Sublingual options include lorazepam and clonazepam
Phenobarbital	Agitation, seizures	• Can be given by G tube as well as rectally, if needed, using the parenteral solution
Antipsychotics	Agitation	• Monitor for side effects
Anticholinergics	Respiratory secretions	• Sublingual options include atropine and hyoscyamine (Levsin)

medications can be helpful. One possibility is to initiate a trial of medication from a different category with a different mechanism of action if symptoms have not improved following two or three dose increases of the current medication. The goal is to provide a reasonable trial while minimizing side effects. The risk of side effects increases as the medication dose is increased.

Opioids

Opioids are covered in detail in chapter 4. Several key points are reviewed here. Opioids can be used to treat pain and dyspnea. Other treatable sources of pain should also be considered, such as bladder distension due to urinary retention, mouth sores (if the mouth is dry), and pressure sores. The typical duration of action of an opioid given by feeding tube or sublingually is 3 to 4 hours, with the peak effect occurring after 1 hour. If scheduled, an opioid should be given every 4 hours. The as-needed dose can be given as often as every hour, prn. Methadone is the exception, as reviewed in chapter 4.

Side effects need to be considered. These include hyperalgesia (being hypersensitive to touch) and myoclonus, which can be mistaken for increasing pain. Side effects should especially be considered if there has been a rapid increase in the opioid dose. Constipation needs to be actively treated, unless death is anticipated within days.

Opioids will not benefit some children with SNI who have pain behaviors at the end of life. Other sources of pain behaviors, such as increasing excitation and decreasing inhibition in the CNS that results in increased tone/spasms/arching, should be considered as a possibility. In general, at the end of life, children who have SNI are more likely to have changes in the CNS that result in features seen with pain, including changes in muscle tone, and less likely to have nociceptive (tissue injury) pain. This does not mean that a child who has SNI will not have pain; it is simply a reminder to keep an open mind when considering the treatment options available.

Benzodiazepines

Benzodiazepines enhance inhibition of the CNS by potentiating the effect of the inhibitory neurotransmitter GABA at the $GABA_A$ receptor. They can be beneficial at the end of life for such problems as increased tone/spasms/arching, agitation, and seizures. They can be used intermittently,

when needed, for such problems as muscle spasms, prolonged seizure, or agitation associated with dyspnea. In addition, they can be scheduled around the clock when these distressing symptoms are frequent or are escalating, without worrying about the tolerance that can occur with prolonged use. At the end of life, scheduled use of benzodiazepines to assist with comfort can be beneficial. Benzodiazepines that can be given buccally include lorazepam and clonazepam.

Phenobarbital

Phenobarbital can provide benefit at the end of life through its ability to increase inhibition and decrease excitation of the CNS. It acts by enhancing the inhibitory action of GABA and inhibiting the excitatory action of glutamate. Phenobarbital has been reported as helpful treatment for persistent agitation as well as seizures in adults at the end of life (Cheng, Roemer-Becuwe, and Pereira 2002; Stirling, Kurowska, and Tookman 1999). Benefit can be seen with the doses used for seizure management and for sedation (Keen 2000). It has also been used for persistent agitation in children who have SNI (Drake and Hain 2006). Phenobarbital can cause paradoxical agitation in some children.

As already noted, an increase in agitation, movement, and arching/stiffening can result from a further imbalance between inhibition and excitation in the CNS. Phenobarbital is a medication to consider when there is an escalation in these features at the end of life despite the use of more commonly selected medications such as opioids and benzodiazepines. Phenobarbital can be given by feeding tube, subcutaneously, or rectally. When given rectally, the parenteral solution is used (Graves et al. 1989).

Antipsychotics (neuroleptics)

The antipsychotic medications, also referred to as neuroleptics, include haloperidol and risperidone. The primary mechanism of action is to block dopamine-2 (D-2) receptors in the brain. These medications have been studied in adults for the treatment of agitation and delirium at the end of life. Their use for children at the end of life is limited by their side effects and by the limited knowledge about their utility for children. Some children may benefit from an empirical trial, though there is no information to suggest a greater benefit over phenobarbital or a benzodiazepine. The potential benefit of antipsychotics must be balanced against their known risks, including agitation and dystonic reactions.

Dyspnea

With respect to dyspnea, the same principles reviewed in chapter 6 are relevant at the end of life. Several points are worth repeating here. The risk for dyspnea will depend on the underlying cause of the child's overall decline; it can be anticipated in a child with declining respiratory function. This is often a time when the goals of care have shifted from disease-modifying care and comfort to an overall goal of comfort, which may include a decision to discontinue interventions—such as antibiotics, chest PT, or mechanical ventilation—that have become too burdensome. When the goal is comfort, morphine sulfate can be effective at treating any associated dyspnea; the medical team can titrate the medication to a dose that improves comfort. Other strategies can lessen problems that contribute to dyspnea, such as stopping tube feedings so as to eliminate the risk of vomiting and excessive fluids in the lungs. This is reviewed in more detail later in the chapter.

At such times, there is a natural fear that morphine will hasten death. The most important point to remember is that the underlying disease is the cause of death, not the use of medications to improve the child's comfort. The medical team can safely increase morphine sulfate when distress increases, such as increasing by 50% for moderate symptoms and by 50% to 100% for severe symptoms. (The case of Jonathan, at the end of chapter 6, highlights the use of morphine sulfate at the end of life.)

For children with an overall decline in CNS function, changes in the respiratory pattern can reflect natural changes that occur at the end of life (as described below, in the section "Signs that death may be approaching").

Respiratory secretions

Respiratory secretions at the end of life can become pronounced and can be distressing for family members. As the ability to cough and clear secretions becomes further impaired, secretions can build up and "rattle" in the chest and at the back of the throat. In addition, children receiving medical fluids and nutrition are at risk for receiving an excessive amount as the body slows down, including decreasing metabolic effort and resulting energy and fluid needs. The result may be extra fluid in the body, including the lungs, noted as an increase in respiratory secretions.

One other risk for developing fluid in the lungs is neurogenic pulmonary edema, which can occur if changes in the hypothalamus cause further

alterations in the autonomic nervous system. Neurogenic pulmonary edema developing at the end of life has been reported in patients with brain tumors and multiple sclerosis (Bramow et al. 2008; Clark and Butler 2009; Macleod 2002). Though it has not been reported in children who have SNI, experience suggests that it may be relevant for a few such patients. Neurogenic pulmonary edema may be indicated by a sudden and significant increase in pulmonary secretions.

Management of distressing secretions at the end of life can include anticholinergic medications and discontinuing the use of medical fluids. Decreasing or discontinuing medical fluids can be a very distressing and emotional decision. (The benefit of this decision is highlighted by the case of Grace, at the end of chapter 6.)

Forgoing artificial nutrition and hydration at the end of life

Over the years, children who have SNI often receive benefit from the use of a feeding tube to provide medical fluid and nutrition. This benefit can decrease and eventually be lost at the end of life. It is distressing to consider how medical feedings can become a source of problems and discomfort. The goal of providing information on this subject here is to improve understanding and to avoid unnecessary complications at the end of life.

Children with feeding tubes are at risk for complications from the continued provision of fluids and nutrition as the body slows down. At such times, the fluid and nutrition needs of the body decrease and, later, the intestines and kidneys become less able to process fluids and nutrition. This can result in vomiting, increased respiratory secretions, and extra fluid in the skin causing puffiness (edema). A person without a feeding tube or IV fluids naturally takes in less as he or she experiences less thirst and less hunger. This declining interest in food and fluid is a protective process at the end of life. A child who has SNI is at increased risk for problems when this natural process is not taken into account. This is a process that can occur gradually over weeks or longer, though for some children it can occur abruptly.

Decreasing or discontinuing medical fluids and nutrition can be one of the most important steps to improve comfort in the last days, weeks, or months of life. The challenge for families and physicians is determining when that time has come. As mentioned in chapter 9, this is a time to consider an empirical trial that involves decreasing or discontinuing medical fluids; there is nothing to lose from such a trial, and useful information to be gained.

It helps to understand the harm from feedings at the end of life and the benefit of the natural release of chemicals that decrease hunger and thirst as the body dehydrates (Casarett, Kapo, and Caplan 2005; Nelson et al. 1995; Stanley 2000; Sullivan 1993). This change reflects the development of ketosis that occurs when fluids and nutrition are stopped. Ketosis results in a loss of appetite and an overall sense of well-being. The benefit of ketosis is lost when nutrition is resumed, including glucose in IV fluids. Adults have described ketosis as a "mild euphoria" when medical fluids and nutrition are no longer given at the end of life (Sullivan 1993). In addition, ketosis can be expected to lessen the risk of seizures at the end of life, based on the benefit of the ketogenic diet for seizure management.

Clearly, then, there is a difference between feeding throughout life and the use of artificial fluids and nutrition that are not tolerated as the body slows down. Decreasing and discontinuing fluids and nutrition can decrease or eliminate fluid in the lungs, the risk of vomiting, and the buildup of fluid in the hands and feet.

The only potential uncomfortable symptom is a dry mouth, which can be alleviated with good mouth care. This can be managed with moistened swabs, careful oral hygiene, and petroleum jelly on the lips.

When medical nutrition and hydration is discontinued because it is prolonging or contributing to suffering, the length of time until death can be 1 to 2 weeks (or shorter, when the function of other organs is declining). It can be longer when fluids are used to flush a feeding tube after giving medications. Changing to sublingual medications, when possible, can lessen the need to flush the feeding tube with water.

Improvement in health following symptom treatment

For some children, health will improve following symptom treatment at a time that is considered "end of life." Families often view such improvement as a "gift," to once again see their child comfortable, with the ability to respond and interact.

A focus on goals, such as shifting from maintaining health to maximizing comfort, can help take the focus away from predicting when a child is dying. A focus on predicting too early what is "end of life" can leave some families uncertain whether they have made the "right" decision to focus on "comfort." It is not that the decision was "wrong," rather that the outcome was better than anticipated by the medical team. This can reflect the difficulty of such predictions and the benefit of symptom treatment on health. It is much more difficult to make decisions based on when a child

with SNI is "dying" rather than based on goals of care, and it can unnecessarily delay a child's comfort. Not all children with SNI have this "honeymoon" period, but it can be a blessing when it occurs.

Nonpharmacological comfort strategies

Many comfort strategies can be provided by families, from the simple to the profound. Comfort can be given by holding a hand or applying lotion to the skin. Providing a quiet and dark environment can be beneficial if a child seems agitated. Often the strategies used throughout life, such as favorite music, can also be beneficial at the end of life. Other interventions can include venting a feeding tube, gently suctioning secretions, and moistening a dry mouth. These acts are important reminders of the benefit of human contact throughout life.

Comfort can also be enhanced by eliminating a treatment that does not enhance comfort—for example, discontinuing the use of monitors, such as a pulse oximeter, which will not change the care plan. Other examples include limiting or stopping the use of respiratory treatments such as chest PT. It can be distressing to consider not using monitoring and care plans that have been part of a child's life for so long. Decisions can be guided by whether the intervention is benefiting the child, interfering with comfort, or prolonging suffering.

SIGNS THAT DEATH MAY BE APPROACHING

Many families want to know, "What should I expect?" and "Is my child near the end of life?" A number of features are commonly observed when someone is near the end of life:

- Increased sleeping; decreased amount of time awake and responsive
- Changes in mental status, such as development of restlessness and agitation
- Noisy breathing with increased airway secretions
- Decreased amount of urine
- Increased swelling of the body (edema), often noted in the arms and legs
- Mottling and cooling of the skin, starting with the hands, feet, arms, and legs
- Cyanosis (bluish or purple coloring) of the skin, starting with the feet and hands

- Changes in the breathing rate and pattern, including Cheyne-Stokes breathing, which is a fluctuating pattern of rapid breathing (tachypnea) or deep breathing followed by a pause in breathing (apnea) that can last 5 to 30 seconds or longer, before a loud deep breath resumes again, and the cycle repeats

Decline in the central nervous system

In children who have SNI, some of the features listed above are seen either intermittently or chronically throughout life. Some children may have a significant episode that appears life-threatening, and then experience the features intermittently, over years. Such an episode may include a significantly lower heart rate and body temperature, decreased alertness, and brief pauses of breathing. A parent may notice such transient and self-resolving episodes occurring sporadically, several times a year, over many years.

What can distinguish these episodes from progressive decline is the frequency of the episodes and the development of new features. When considering how long a child might live when such changes are noted, the following might be a useful guideline: if a child is experiencing decline with new changes that are now occurring monthly, he or she may have months to live; if weekly, weeks to live; and if daily, days to live. This is just a guideline for preparing and does not mean a child will die in that time frame.

Many of the changes noted at the end of life can result from alterations in the CNS. In general, such changes in children who have SNI indicate changes in the lower centers of the brain, including the hypothalamus, pons, and medulla. Changes can include a decrease in alertness, slowing of the heart rate and intestinal function, lowering of body temperature, changes in the respiratory pattern with episodes of apnea, and mottling of the hands and feet. Some children "just have their whole systems slow down and die." (The case of Jonathan illustrates such changes.)

Decline as a result of progressive alterations in the CNS is expected in neurodegenerative diseases. Such changes can also be observed in children with "static" disorders of the brain. This may result from neuronal apoptosis (cell death of the nerve cells) in the setting of severe preexisting impairment of the CNS (Hotchkiss et al. 2009).

These changes may reflect alterations in the centers of the brain that regulate arousal, heart rate, blood pressure, body temperature, respiratory function, and intestinal function. Changes in the CNS might also further alter the balance between inhibition and excitation. Problems that may then increase, as noted earlier, include muscle spasms, abnormal movement,

arching, stiffening, seizures, agitation, and central pain. Medications can be selected that either enhance inhibition or decrease excitation of signals.

Physical changes as death is near

For some children, the end-of-life changes described above occur gradually, over months. For other children, the end of life will reflect decisions to discontinue life-sustaining treatment as the goals of care shift. Parents often wonder "how long," as they prepare for the unthinkable, the death of their child.

Information can help parents prepare for changes in the physical appearance of their child's body. This includes the changes listed at the beginning of this section. Changes in the breathing pattern can make parents worry that their child is "struggling" to breathe. When such changes occur, a child is unaware of what is happening. As the carbon dioxide in the body builds up, the body takes deeper breaths. This increase in carbon dioxide is naturally sedating, like an anesthetic for the body. Following this, there can be pauses in breathing followed by a deep breath. This, again, is not uncomfortable or distressing for the child. These pauses become longer just before death. Other changes are typically noted at this time, including the hands and feet becoming mottled, blue, and cool.

Parents may also wish to prepare for the "when" so that they can be with their child at the time of death. There are two themes that seem to emerge. Some children seem to "stay with" their family until their death, until they are "given permission" to pass. For other families, their child "waited" until they were away from the room. It is hard to predict "when," as gradual changes can shift to a sudden decline in some children. What is constant throughout this time is the opportunity for families to bring statements of love to their child as the end of life is near.

GRIEF AND BEREAVEMENT

What many people don't realize is that when you have a child with complex health care needs, grieving is part of the process of life. We grieve the life we had hoped for them. We grieve the milestones they don't hit. We grieve when they can't use an age-appropriate toy again and again, one birthday after another. We grieve on days that don't necessarily make sense. Grief is quite simply part of life.

—Deborah Tiel Millard

Parents of children who have SNI live with many losses, as poignantly described above by a parent. What is unthinkable is grieving the loss of a child. Parents describe the intensity of feelings that can be unbearable at times. They also describe how, over time, "you begin to think more about the happy times." "Grieving a child really is part of your life with that child. You will always carry your child with you, as part of you" (Millard 2010).

The days, weeks, and months following the loss of a child can be a rollercoaster of intense feelings: shock, despair, anger, loneliness, yearning, physical sensations, loss of energy, irritability, and listlessness are just a few. The process of grieving may initially seem impossible, yet most parents eventually work through the part that feels unbearable (Barrera et al. 2007; Kreicbergs et al. 2007). This is not the same as *getting over* the loss. In fact, the ability to maintain a continued bond with a deceased child is beneficial to parental bereavement and adjustment (Barrera et al. 2007). Grieving can be a process of integrating a child's memory into a new reality. Thomas Attig (1996) has poignantly described this as a process of "relearning the world."

Factors that can help during the grieving process include parents sharing their problems with others during the child's illness, parents having access to psychological support during the last month of their child's life, and counseling offered by healthcare staff during the child's last month of life (Kreicbergs et al. 2007). Grieving starts before a child's death and can involve preparing for that death. This has been referred to as "anticipatory mourning," the process of emotional preparation leading up to the time of death (Rini and Loriz 2007).

Anticipatory grieving may at first seem conflicting: showing that you will not "give up" while being asked to prepare for your child's death. Some families see this as a continuum of the work they have always done on behalf of their child. Some of the work has a direct impact on their child's life; the other work honors their child's life.

Siblings also benefit from opportunities to explore the experience of having a brother or sister with serious health problems. Opportunities can include involving siblings throughout the illness trajectory, allowing them to have safe outlets for their feelings, and creating opportunities for their needs to be identified and met. All of these steps have proven useful to later bereavement (Davies 1999).

Parents and siblings can be supported before and following their loss. Resources can be accessed through the community, including through palliative care and hospice programs. Bereavement programs are found to

be beneficial. Children and parents have described the benefit of the freedom to express themselves, a diminished sense of isolation, and the normalization of their emotions (Davies et al. 2007; Wilkinson et al. 2007). Parents have described using a bereavement support service for advice and reassurance, for support for their children while they grieved, and for advice on addressing behavioral difficulties at home and school. Even those who did not use the service said it was helpful to know that the service existed.

The limited research has not found differences in measures of grief between parents of children with developmental impairment and other parents after their child's death (Reilly et al. 2008). Yet unique areas of bereavement are seen in parents of children with developmental disabilities; these include the parents' loss of an intensive caregiver role and support group membership; their lack of opportunity to share their grief, resulting in a "socially imposed" silent grief; and conflicting feelings of sadness and relief over prior fears about the child's future.

Grief is a process that never goes away, yet it changes over time. As described by one parent, "In the early months, finding ways to actively remember and mourn Sebastian helped me to get through the days. Later, these rituals and traditions became ways to celebrate his life and include him in our ongoing family life. My journey has been harder than I could have imagined, and yet filled with many blessings and much joy. I am immensely grateful for having had Sebastian in my life, and I want to remember and honor him each and every day" (Gray 2010).

References

Attig T. 1996. *How We Grieve: Relearning the World.* New York: Oxford University Press.

Barrera M, D'Agostino NM, Schneiderman G, et al. 2007. Patterns of parental bereavement following the loss of a child and related factors. *Omega (Westport)* 55(2):145–67.

Birnbaum AK, Kriel RL, Im Y, Remmel RP. 2001. Relative bioavailability of lamotrigine chewable dispersible tablets administered rectally. *Pharmacotherapy* 21(2):158–62.

Bramow S, Faber-Rod JC, Jacobsen C, et al. 2008. Fatal neurogenic pulmonary edema in a patient with progressive multiple sclerosis. *Mult Scler* 14(5):711–15.

Casarett D, Kapo J, Caplan A. 2005. Appropriate use of artificial nutrition and hydration—fundamental principles and recommendations. *N Engl J Med* 353(24):2607–12.

Cheng C, Roemer-Becuwe C, Pereira J. 2002. When midazolam fails. *J Pain Symptom Manage* 23(3):256–65.

Clark K, Butler M. 2009. Noisy respiratory secretions at the end of life. *Curr Opin Support Palliat Care* 3(2):120–24.

Davies B. 1999. *Shadows in the Sun: The Experiences of Sibling Bereavement in Childhood.* Philadelphia: Taylor and Francis.

Davies B, Collins J, Steele R, et al. 2007. Parents' and children's perspectives of a children's hospice bereavement program. *J Palliat Care* 23(1):14–23.

Drake R, Hain R. 2006. Pain—pharmacologic management. In *Oxford Textbook of Palliative Care for Children*, ed. Goldman A, Hain R, Liben S, pp. 325–26. Oxford: Oxford University Press.

Dussel V, Kreicbergs U, Hilden JM, et al. 2009. Looking beyond where children die: determinants and effects of planning a child's location of death. *J Pain Symptom Manage* 37(1):33–43.

Epilepsy.com. 2011. AEDs for rectal administration. http://professionals.epilepsy.com/page/table_procedures_rectal.html.

Graves NM, Holmes GB, Kriel RL, et al. 1989. Relative bioavailability of rectally administered phenobarbital sodium parenteral solution. *DICP* 23(7–8):565–68.

Gray E. 2010. Remembering Sebastian with joy: rituals of remembrance. *Complex Child E-Magazine.* www.articles.complexchild.com/july2010/00218.html.

Hotchkiss RS, Strasser A, McDunn JE, Swanson PE. 2009. Cell death. *N Engl J Med* 361(16): 1570–83.

Keen JC. 2000. Re: the use of phenobarbitone in the management of agitation and seizures at the end of life. *J Pain Symptom Manage* 19(2):80–81.

Kreicbergs UC, Lannen P, Onelov E, Wolfe J. 2007. Parental grief after losing a child to cancer: impact of professional and social support on long-term outcomes. *J Clin Oncol* 25(22):3307–12.

Macleod AD. 2002. Neurogenic pulmonary edema in palliative care. *J Pain Symptom Manage* 23(2):154–56.

Millard DT. 2010. A process of grief: the reality of grieving a child with complex health care needs. *Complex Child E-Magazine.* http://articles.complexchild.com/july2010/00220.html.

Nelson LJ, Rushton CH, Cranford RE, et al. 1995. Forgoing medically provided nutrition and hydration in pediatric patients. *J Law Med Ethics* 23(1):33–46.

Reilly DE, Hastings RP, Vaughan FL, Huws JC. 2008. Parental bereavement and the loss of a child with intellectual disabilities: a review of the literature. *Intellect Dev Disabil* 46(1):27–43.

Rini A, Loriz L. 2007. Anticipatory mourning in parents with a child who dies while hospitalized. *J Pediatr Nurs* 22(4):272–82.

Smith S, Sharkey I, Campbell D. 2001. Guidelines for rectal administration of anticonvulsant medication in children. *Paediatr Perinat Drug Ther* 4(4):140–47.

Stanley AL. 2000. Withholding artificially provided nutrition and hydration from disabled children: assessing their quality of life. *Clin Pediatr* 39(10):575–79.

Stirling LC, Kurowska A, Tookman A. 1999. The use of phenobarbitone in the management of agitation and seizures at the end of life. *J Pain Symptom Manage* 17(5):363–68.

Sullivan RJ Jr. 1993. Accepting death without artificial nutrition or hydration. *J Gen Intern Med* 8(4):220–24.

Wilkinson S, Croy P, King M, Barnes J. 2007. Are we getting it right? Parents' perceptions of hospice child bereavement support services. *Palliat Med* 21(5):401–7.

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Glossary

advance care planning Planning in advance of a life-threatening event to ensure that only the interventions that are agreed upon in advance will be used

agitation An unpleasant state of arousal indicated by irritability, restlessness, and increased motor activity

agonists Medications that stimulate receptors

akathisia An unpleasant sensation of inner restlessness that can be caused by dopamine antagonists, selective serotonin reuptake inhibitors, and tricyclic antidepressants

allodynia Pain from a stimulus that does not normally cause pain

allow natural death (AND) Indicates that treatment is focused on keeping a child comfortable and protecting him or her from treatments that are not likely to have benefit; the term reflects a focus on what is being done rather than on what is being avoided

alveoli Air sacs in the lungs; the areas where gas exchange of oxygen and carbon dioxide takes place between the lungs and the capillaries (smallest blood vessels)

amenorrhea Absence of a menstrual period

antagonists Medications that block receptors

anthropometric measures Comparative measures of the body that are used to assess nutritional status, such as weight-for-length percentile or body mass index (BMI)

anticholinergics Medications that block the acetylcholine receptor; include glycopyrrolate, oxybutynin, scopolamine, hyoscyamine, and atropine

antiemetics Medications that decrease vomiting and retching, typically by blocking receptors that stimulate the vomiting reflex

antiepileptic drugs (AEDs) Medications for the treatment of epilepsy (recurrent seizures)

anti-reflux surgery (ARS) Surgical tightening of the junction between the stomach and esophagus; Nissen fundoplication is a specific type of ARS

apnea *See* central apnea; obstructive sleep apnea

apoptosis Cell death

artificial nutrition and hydration Nutrition and fluids that are medically provided by a feeding tube or by an intravenous line

aspiration Passage of foreign material such as food, stomach contents, and saliva into the airways and lower respiratory tract

atelectasis The collapse of air sacs (alveoli) resulting in reduced or absent exchange of oxygen and carbon dioxide within the air sacs of the lungs, often the result of a mucus plug

autonomic dysfunction Impairment in the areas of the central nervous system that regulate the autonomic nervous system; these areas include the hypothalamus, pons, and medulla oblongata

autonomic nervous system The branch of the nervous system involved in regulation of involuntary functions in the body, including body temperature, heart rate, blood pressure, respiration rate, intestinal motility, urination, salivation, perspiration, and the diameter of the pupils

basal ganglia A group of nerve cells (nuclei) that are involved in the voluntary control of movement, through connections to the cerebral cortex, thalamus, and other areas of the central nervous system

bereavement The state of having suffered a loss and the experiences that follow the death of a loved one

bilevel positive airway pressure (BiPAP) A form of noninvasive positive airway pressure ventilation that is delivered through a mask that fits tightly on the face

body mass index An indirect indicator of body fat, based on an individual's weight and height

bone mineral density (BMD) The amount of mineral content in the bones, used as an indirect indicator of osteoporosis and bone fracture risk

bradycardia Low heart rate

brain stem *See* medulla oblongata; midbrain; pons

bronchiectasis The development of abnormal permanent dilation of the bronchi

bronchioles Passageways in the lungs through which air moves from the nose/mouth to the air sacs (alveoli)

bronchospasm A sudden constriction of the muscles in the walls of the bronchioles (the airways in the lungs)

buccal Delivery route for medication, placed between the gum and the cheek

cardiac arrest The heart has stopped (no pulse)

cardiopulmonary function Function of the heart and lungs

cardiopulmonary resuscitation (CPR) An attempt to restart breathing and the heart when a person has stopped breathing or the heart has stopped (referred to as cardiopulmonary arrest)

central apnea Diminished or absent respiratory effort that occurs in an intermittent or cyclical fashion as a result of impairment in the respiratory centers of the brain (medulla and pons)

central nervous system (CNS) The brain and spinal cord

central pain Neuropathic pain resulting from impairment in the central nervous system in the area of the spinothalamic tract

cerebral palsy Nonprogressive impairment of the central nervous system affecting muscle tone and control of movement

cerebral salt wasting (CSW) Low serum sodium level (hyponatremia) resulting from excessive excretion of sodium into the kidneys, resulting from damage to the central nervous system

chest physiotherapy (chest PT) Interventions used to assist in mucus clearance from the lungs

cholecystitis Inflammation of the gallbladder

chorea Abrupt, irregular, chaotic, involuntary movements that can range from tiny fidgeting to more obvious dance-like movements that flow from body part to body part

clonus Involuntary muscle contractions due to sudden stretching of the muscle, most commonly seen at the ankle

***Clostridium difficile* (C. diff.)** A bacterium that can cause diarrhea and inflammation of the colon when competing bacteria in the intestines (referred to as normal gut flora) have been altered by antibiotics

comfort care Treatment that is focused on maintaining or improving comfort

computed tomography (CT) A medical imaging procedure that utilizes X-rays to generate cross-sectional pictures of the body area scanned

constipation Infrequent passage of stool

continuous positive airway pressure (CPAP) A form of noninvasive positive airway pressure ventilation that is delivered through a mask that fits tightly on the face

cortisol deficiency *See* glucocorticoid deficiency

decerebrate posturing Rigidity, bending (flexion) of the arms, clenched fists, and extended legs

decorticate posturing Rigid straightening (extension) of the arms and legs, downward pointing of the toes, and backward arching of the head

deep vein thrombosis (DVT) A blood clot in a deep vein, most commonly in a leg

delirium Disturbance of consciousness with an acute onset over hours to days and a fluctuating course

dementia A serious loss of cognitive (intellectual) ability in a previously unimpaired individual, seen with neurodegenerative conditions such as certain metabolic diseases

DEXA (or DXA) scan *See* dual emission X-ray absorptiometry

diarrhea Loose, more frequent bowel movements (stool)

discontinuing medical treatment Stopping an intervention that is no longer meeting the goals of care, such as when an intervention is prolonging suffering

do not attempt resuscitation (DNAR) The same as DNR, with the addition of *attempt* as a reminder that resuscitation is an attempt at restoring heart function and breathing that is not effective in all patients

do not intubate (DNI) A decision not to use intubation

do not resuscitate (DNR) A decision not to use cardiopulmonary resuscitation

dopamine antagonists Medications that block dopamine receptors; include metoclopramide and risperidone

drooling (sialorrhea) Thin, watery secretions that can pool out of the mouth, resulting from a diminished oral sensation of saliva

dual emission X-ray absorptiometry (DEXA or DXA) A test that measures bone density

DXA (or DEXA) scan *See* dual emission X-ray absorptiometry

dysautonomia *See* autonomic dysfunction

dyspnea The experience of shortness of breath, difficulty of breathing, breathlessness, or uncomfortable breathing

dystonia A movement disorder in which involuntary sustained or intermittent muscle contractions cause twisting, repetitive movements, and abnormal postures

dystonic reactions Abnormal movements as a result of medication toxicity, such as from metoclopramide and risperidone; features include involuntary contractions of muscles in the face (with grimacing, tongue protrusion, lip smacking, puckering of the lips, and rapid eye blinking), neck, trunk, and extremities

electrocardiogram (ECG or EKG) A test that records the electrical activity of the heart, used to diagnose abnormal rhythms of the heart

electroencephalogram (EEG) A test that records the electrical activity of the brain, used by neurologists in the evaluation of epilepsy

emetic reflex *See* vomiting reflex

empirical treatment A decision to use a treatment (1) based on experience indicating the potential for benefit or (2) before the results of a test are available; examples include medications for symptom treatment, treatment of gastroesophageal reflux disease, and antibiotic selection for bacterial infections (with or without a bacterial culture test)

enteric nervous system A network of nerves in the gut, partly controlled by the central nervous system through the autonomic nervous system

epilepsy A condition in which a person has two or more seizures that are not provoked by specific events, such as low blood glucose

esophagitis Inflammation of the esophagus, such as from gastroesophageal reflux disease

esophagogastric disconnection A surgery that disconnects the esophagus from the stomach and reattaches the esophagus to the small bowel (intestine)

evidence-based medicine (EBM) A method that seeks to assess the strength of evidence that helps us understand the risks and benefits of diagnostic tests and treatment options

extrapyramidal symptoms Movement disorders such as acute dystonic reactions and akathisia that can be secondary to the use of dopamine antagonists, including metoclopramide and risperidone

family-centered care Care delivery that involves collaboration among patients, families, physicians, nurses, and other professionals for the planning, delivery, and evaluation of healthcare

feeding intolerance The persistent inability to tolerate a calculated volume of nutrition and fluids given into the gastrointestinal tract, whether by gastrostomy or jejunostomy tube, despite multiple interventions

fever *See* hyperthermia

forgoing medical treatment Not initiating a medical intervention that has a higher likelihood of causing harm rather than benefit and is not consistent with the identified goals of care, such as an intervention that will cause or prolong suffering

fracture A break in a bone

gastritis Inflammation of the stomach lining

gastroesophageal reflux (GER) The effortless movement of gastric content across the lower esophageal sphincter (LES) into the esophagus

gastroesophageal reflux disease (GERD) Chronic gastroesophageal reflux leading to tissue inflammation, injury, and symptoms

gastrointestinal (GI) motility The ability to propel content in the stomach and intestines forward by means of coordinated contractions of the smooth muscle in the GI tract

gastrointestinal (GI) tract The stomach and intestines; also called the gut, bowels, and intestines

gastrostomy feeding tube (G tube) A tube placed through the abdominal wall into the stomach for the purpose of providing medications, fluid, and nutrition

glucocorticoid deficiency Inadequate corticosteroid (cortisol) release from the adrenal gland, such as when the brain does not have adequate hormone secretion from the hypothalamus or pituitary gland to stimulate cortisol release from the adrenal gland

goals of care The views, beliefs, and values that influence and guide medical decision making

gray matter The nerve cells (neurons) in the brain

grief A person's response to and experience of loss

growth attenuation The use of high-dose estrogen to minimize the final length/height of a child

growth hormone deficiency Inadequate production of growth hormone

hematemesis Vomiting of material that contains blood

hepatotoxicity Damage to the liver, such as from medications

high-frequency chest wall oscillation *See* pulmonary vest

hope An adaptive response to a stressful circumstance, allowing a person to cope

hospice A continuation of the philosophy of palliative care that includes support of care at the end of life, typically community-based rather than hospital-based

hyperalgesia An increased response to a painful stimulus causing a higher level of pain

hypernatremia Elevated sodium level, typically a result of excessive water loss from the body

hyperthermia Elevated body temperature

hypertonia Increased resistance of muscle to externally imposed movement (referred to as passive movement) that is not dependent on the velocity (speed) of movement

hyponatremia Low serum sodium as measured in the blood, defined as a serum sodium of less than 135 mEq/L

hypothalamus An area of the brain located in the midline, involved in the control of heart rate, blood pressure, body temperature, and sleep-wake cycles, as well as in endocrine function that is linked to the hypothalamus, including thyroid function, water and sodium regulation, steroid (cortisol) release, and pubertal development

hypothermia Low body temperature, defined as a temperature below 95 °F (35 °C)

hypothyroidism Inadequate thyroid hormone release from the thyroid gland, such as when the brain does not have adequate hormone secretion from the hypothalamus or pituitary gland to stimulate release of thyroid hormone from the thyroid gland

inborn errors of metabolism *See* metabolic diseases

informed consent The requirement to disclose the pros and cons of an intervention, as well as review alternative options

insufflator-exsufflator cough production device (CoughAssist) A machine that simulates a cough by applying positive pressure into the airway, followed rapidly by negative pressure

integrative therapies *See* nonpharmacological symptom management

intensive care unit (ICU) A specialized unit of the hospital that provides medical care to patients with the most serious illness; for example, used when patients require mechanical ventilation, intravenous medications to maintain blood pressure, and constant monitoring

intractable epilepsy Continued seizures despite multiple medication trials; also called refractory epilepsy

intractable symptoms Symptoms that persist despite the use of interventions to treat potential contributing problems as well as medications that target specific symptoms

intrathecal baclofen (ITB) pump A treatment for spasticity, with the surgical placement of a pump that delivers baclofen as a continuous infusion into the intrathecal space of the spinal cord

intravenous (IV) Delivery route involving the infusion of fluids and medications directly into a vein through a venous catheter, typically through peripheral veins of the hands and arms, and less commonly through central veins in the chest

intubation Placement of a flexible plastic tube into the trachea (windpipe) so as to maintain an open airway and to facilitate ventilation of the lungs, including the use of a ventilator (respirator)

jejunostomy feeding tube (J tube) A feeding tube that allows feedings to bypass the stomach by directly entering the jejunum, the upper portion of the intestines

life-sustaining medical treatment All medical interventions that may prolong the life of a patient, including respirators, antibiotics, chest physiotherapy, and nutrition and hydration provided intravenously or by feeding tube

magnetic resonance imaging (MRI) Specialized medical imaging that allows detailed pictures of the internal structures in the body, without the use of X-rays

mechanical ventilation (ventilator) The use of a device to artificially support respiratory function, either in the short term or chronically

medical home A model of care delivery that is accessible, continuous, comprehensive, family-centered, coordinated, compassionate, and culturally effective

medical nutrition and hydration Fluids and nutrition that are provided medically, such as by a feeding tube (e.g., a gastrostomy tube) or by an intravenous line (referred to as parenteral nutrition)

medulla oblongata An area of the brain located in the brain stem, below the pons, that is involved in the regulation of breathing, heart rate, blood pressure, swallowing, and vomiting

menarche Menstruation or menstrual period

metabolic diseases Diseases that can result in progressive and degenerative damage to the brain by interfering with the normal enzymatic or metabolic pathways that are essential to the function of cells; also called inborn errors of metabolism

metabolic rate The energy expenditure of a person, which is the amount of calories burned off; typically lower in children with severe neurological impairment

midbrain An area of the brain located between the thalamus/hypothalamus and the brain stem, involved in the regulation of vision, hearing, motor control, sleep-wake cycles, arousal (alertness), and temperature

motility *See* gastrointestinal motility

mourning Outward expression of grief, in addition to cultural and religious customs and rituals surrounding death; the process of adapting to loss and adjusting to the death of a loved one

mucolytic agents Interventions that may help loosen and thin secretions; they are most effective in patients with cystic fibrosis and less effective for other conditions of the lungs

mucus mobilization Interventions that enhance the clearance of mucus (secretions) from the lungs in individuals with impaired cough

mucus plug A blockage in the lungs caused by mucus (secretions in the lungs)

muscle spasms Sudden involuntary contractions of a muscle or group of muscles

myoclonus Brief, abrupt, shock-like, nonsuppressible, involuntary movements that are due to sudden contraction or relaxation of one or more muscles

nausea A feeling of sickness in the stomach characterized by an urge to vomit

nephrolithiasis Kidney stones

neurodegeneration Ongoing injury to the central nervous system as a result of an underlying disease or other factors, such as anesthesia, that can result in cell death (apoptosis) of nerve cells (neurons)

neuroleptics Medications used to treat delirium and severe agitation that does not improve with other interventions; also called antipsychotic medications; risperidone is an example

neuromuscular scoliosis Curvature of the spine due to change in control of the nerves or muscles that support the spine

neurons Nerve cells in the central nervous system

neuropathic pain Pain due to damage to the nervous system that results in abnormal transmission of pain signals and does not involve ongoing tissue injury

neurotransmitters Chemicals that activate or inhibit receptors on nerve cells (neurons), allowing the nerve cells to transmit signals through the nervous system; examples are acetylcholine, dopamine, GABA (gamma-aminobutyric acid), glutamate, and serotonin

Nissen fundoplication *See* anti-reflux surgery

nociceptive pain A normal and expected pain response to injury or inflammation of tissue in the body; it warns of tissue damage through specialized nerve endings that send pain messages from the site of injury to the central nervous system

nonpharmacological symptom management Interventions, other than medications, that improve comfort

number needed to treat (NNT) A number used to compare the relative benefit of one treatment over another

obstructive sleep apnea Obstruction of the upper airway that disrupts normal airflow during sleep and thus disrupts normal sleep

opisthotonos Rigidity and severe arching of the back, with the head thrown backward

osteoporosis Condition indicated by a bone mineral density that is significantly below the expected level for an average, healthy individual

pain An unpleasant sensory and emotional experience associated with actual or potential tissue damage

pain behaviors Features (behaviors) that are observed when a nonverbal child with severe neurological impairment is experiencing pain

palliative care An approach to care that seeks to improve the quality of life of patients who have life-threatening conditions and their families; supports all treatment options, whether disease-modifying or focused on comfort

pancreatitis Inflammation of the pancreas that can be caused by medications and by prolonged hypothermia (low body temperature)

paradoxical reactions Unexpected responses to medications, such as the development of agitation and restlessness from a medication that is typically sedating when first used; can be seen with benzodiazepines, antihistamines, and anticholinergics

parenteral nutrition Nutrition and hydration provided by an intravenous line

peristalsis Contraction and relaxation of smooth muscles in the intestinal tract, resulting in forward movement of intestinal content

philosophy of care An approach to decisions that represents the general values and preferences of a family

Physician Orders for Life Sustaining Treatment (POLST) A form available in some states that allows preferences for life-sustaining treatment to be both documented and honored across different care settings, including the hospital, home, and long-term care

pneumonia Inflammation of the lungs due to infection and chemical irritants, such as aspiration of oral secretions

polypharmacy The use of multiple medications, increasing the risk of drug interactions and side effects

polysomnogram Sleep study for the assessment of obstructive or central apnea

pons An area of the brain located in the brain stem, involved in the regulation of sleep, breathing, swallowing, bladder function, eye movement, facial expressions, and the secretion of saliva and tears

postictal period The time period following a seizure, often with an altered level of alertness

posturing Involuntary flexion (bending) or extension (straightening) of the extremities, often with associated arching

precocious puberty The onset of pubertal changes at an age that is earlier than expected

premature adrenarche The early secretion of adrenal androgens, resulting in the premature appearance of pubic hair (pubarche); typically a benign finding

premature thelarche A benign condition manifested by isolated breast development before puberty

prn Medication used when needed (from *pro re nata*, "as the circumstance arises")

progressive impairment of the central nervous system Ongoing injury to the central nervous system as a result of the underlying disease

prokinetic (promotility) medications Medications that can enhance gastrointestinal motility (forward movement)

prolonged QT interval An interval measured by an electrocardiogram (ECG or EKG) that, because it is prolonged, results in an increased risk of developing an abnormal heart rhythm that can be life-threatening

pseudo-obstruction Ineffective intestinal propulsion characterized by features of intestinal obstruction but in the absence of a mechanical blockage in the intestinal tract

puberty The process of physical changes in a child's body as it matures into an adult body, as a result of hormonal stimulation

pulmonary edema Excessive fluid in the lungs

pulmonary embolism Caused when a blood clot in a deep vein breaks off and travels to the lungs, resulting in blockage of a blood vessel in the lung

pulmonary fibrosis Development of scar tissue in the lungs

pulmonary vest A mechanical device to assist with clearance of mucus from the lungs, by a process referred to as high-frequency chest wall oscillation

QT interval An interval measured by an electrocardiogram (ECG or EKG), associated with the risk of an abnormal heart rhythm when prolonged

refractory epilepsy *See* intractable epilepsy

regurgitation Effortless return of small amounts of food or secretions to the mouth

respiratory arrest Breathing has stopped

respiratory depression The slowing of breathing, often noted as a decrease in the rate of breathing (respiratory rate)

respiratory distress *See* dyspnea

respiratory exacerbation Acute respiratory illness in a child with severe neurological impairment that results from multiple contributing factors, including impaired cough, microaspiration of saliva, chronic inflammation, mucus plugs, atelectasis, and secondary infection (pneumonia)

respiratory failure Inadequate gas exchange by the respiratory system, resulting in blood oxygen (O_2) and/or carbon dioxide (CO_2) levels that cannot be maintained within the normal ranges necessary to support life and avoid complications; respiratory failure can progress to respiratory arrest

restrictive lung disease Reduction in the total lung volume, such as from neuromuscular scoliosis (curvature of the spine that reduces lung expansion)

resuscitation status Documented decisions about the use of resuscitation (CPR) and intubation

retching The first phase of the vomiting reflex, which involves the same mechanisms as vomiting but without ejection of stomach contents; also called gagging or dry heaves

seizure A sudden abnormal electrical discharge in the brain that can result in physical movements, an alteration in consciousness, or a combination of symptoms

selective serotonin reuptake inhibitors (SSRIs) Medications that inhibit the reuptake of serotonin; used in the treatment of depression; less effective than serotonin-norepinephrine reuptake inhibitors in treating neuropathic pain

serotonin-norepinephrine reuptake inhibitors (SNRIs) Medications that inhibit the reuptake of serotonin and norepinephrine; used in the treatment of peripheral and central neuropathic pain, as well as depression

severe neurological impairment (SNI) In this book, refers to children and young adults who have severe impairment of the central nervous system (brain) that is acquired in childhood

shared decision making The need to have both physicians and families share information, express preferences, take steps to build consensus toward a decision, and reach an agreement on a treatment plan

shortness of breath *See* dyspnea

sialorrhea *See* drooling

spasticity A specific type of hypertonia, with an involuntary, velocity-dependent increase in muscle tone such that muscles are resistant to movement

spinal reflex Movement that is under the control of the spinal cord without involvement of the brain, in response to a stimulus; can be seen in persistent vegetative state

spinothalamic tract The area of the central nervous system involved in transmitting information about pain; when impaired, it can result in central neuropathic pain

static impairment of the central nervous system Impairment that is the result of an event or a condition that does not directly cause further damage to the central nervous system

status epilepticus A constant or near-constant state of prolonged seizure, often defined as lasting more than 30 minutes

sublingual Delivery route for medication, placed under the tongue

superior mesenteric artery syndrome Mechanical obstruction of the gastrointestinal tract resulting from compression of the upper part of the intestine (duodenum) between the abdominal aorta to the back and the superior mesenteric artery to the front; risk factors include sudden weight loss and following spinal surgery

symptom treatment Treatment to decrease distressing symptoms that may involve blocking transmission or perception of a symptom, rather than eliminating the cause of the symptom

syndrome of inappropriate antidiuretic hormone (SIADH) The inappropriate, persistent release of antidiuretic hormone (also called vasopressin) resulting in a decrease in the excretion of water from the kidneys, often leading to a low serum sodium level (hyponatremia)

tachycardia Elevated heart rate

thalamus A midline, paired, symmetrical structure located between the cerebral cortex and the midbrain that is involved in the processing of sensory signals from the body (somatic) and from the gastrointestinal tract and bladder (visceral), as well as in regulating states of sleep and arousal (alertness)

time-limited trial An agreement between the medical team and the family to use an intervention over a defined time period

tracheal separation Surgical separation of the trachea (windpipe) into an upper section, which remains a blind pouch or is connected to the esophagus, and a lower section that becomes the new airway with a tracheostomy tube

tracheotomy Creation of an airway through the neck into the trachea (windpipe) with placement of a tracheostomy tube; *tracheotomy* and *tracheostomy* are often used interchangeably

tricyclic antidepressants (TCAs) Medications that inhibit the reuptake of serotonin and norepinephrine; used in the treatment of visceral hyperalgesia, peripheral and central neuropathic pain, and depression; examples include amitriptyline and nortriptyline

urinary tract infection (UTI) A bladder infection

vagus nerve A nerve with functions that include transmission of information between the brain and the viscera (including the esophagus, stomach, and

intestines), to provide control of gastrointestinal (GI) motility and sensory input from the GI tract back to the brain, and between the brain and the heart, involving regulation of heart rate

vegetative state A state with cycles of eye opening and closing that give the appearance of sleep-wake cycles, complete lack of awareness of the self or the environment, and complete or partial preservation of hypothalamic and brain stem autonomic functions

ventilation perfusion (V/Q) mismatch A mismatch or imbalance in the areas of the lung available for the exchange of oxygen and carbon dioxide with the capillaries (smallest blood vessels)

videofluoroscopic swallow study (VSS) An assessment of swallowing and of the possible presence of aspiration

visceral hyperalgesia An altered response to stimulation of the intestines, resulting in a decreased threshold for pain generation in response to a stimulus

vomiting Forceful ejection of stomach contents through the mouth as a result of spasmodic, involuntary contractions of the intestinal tract, abdomen, and diaphragm

vomiting center Brain center located in the medulla oblongata; when stimulated, results in retching and vomiting

vomiting reflex The process that results in vomiting through stimulation of the receptors in the vomiting center; also called the emetic reflex

white matter The myelinated nerve fibers that conduct electrical impulses between nerve cells

***z* score** For a measured feature, the number of standard deviations above or below the average (mean) as compared with others of the same age, sex, and race/ethnicity

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